(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 April 2003 (17.04.2003)

PCT

(10) International Publication Number
WO 03/031588 A2

(51) International Patent Classification[7]: C12N

(21) International Application Number: PCT/US02/32512

(22) International Filing Date: 10 October 2002 (10.10.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/328,655 11 October 2001 (11.10.2001) US
60/363,774 13 March 2002 (13.03.2002) US

(71) Applicants *(for all designated States except US)*: **MERCK & CO., INC.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P. ANGELETTI, S.P.A.** [IT/IT]; VIA PONTINA KM. 30.600, I-00040 POMEZIA (IT).

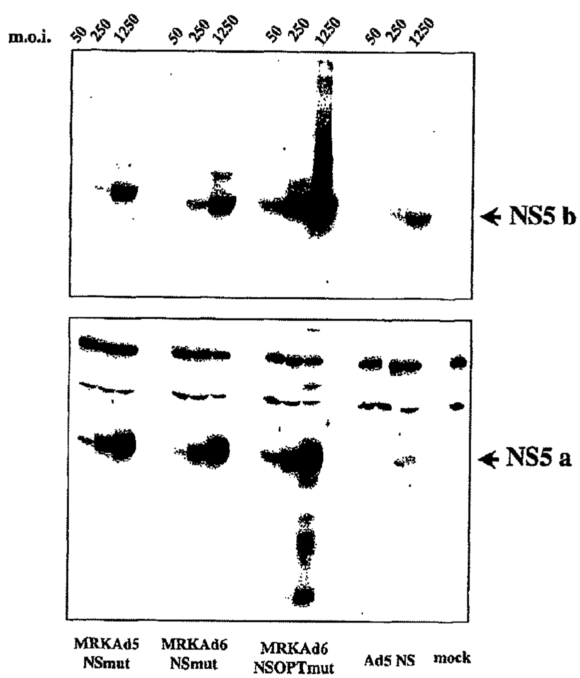
(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **EMINI, Emilio, A.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **KASLOW, David, C.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **BETT, Andrew, J.** [CA/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **SHIVER, John, W.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **NICOSIA, Alfredo** [IT/IT]; Via Pontina KM. 30.600, I-00040 Pomezia (IT). **LAHM, Armin** [DE/IT]; Via Pontina KM. 30.600, I-00040 Pomezia (IT). **LUZZAGO, Alessandra** [IT/IT]; Via Pontina KM. 30.600, I-00040 Pomezia (IT). **CORTESE, Riccardo** [IT/IT]; Via Pontina KM. 30.600, I-00040 Pomezia (IT). **COLLOCA, Stefano** [IT/IT]; Via Pontina KM. 30.600, I-00040 Pomezia (IT).

(74) Common Representative: **MERCK & CO., INC.**; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

[Continued on next page]

(54) Title: HEPATITIS C VIRUS VACCINE



Western blot on whole-cell extracts from HeLa cells infected at different multiplicity of infection (m.o.i.; indicated at the top) with Adenovectors expressing the different HCV NS cassettes. Mature NS5B and NS5A products were detected with specific antibodies.

(57) Abstract: The present invention features Ad6 vectors and a nucleic acid encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide containing an inactive NS5B RNA-dependent RNA polymerase region. The nucleic acid is particularly useful as a component of an adenovector or DNA plasmid vaccine providing a broad range of antigens for generating an HCV specific cell mediated immune (CMI) response against HCV.

WO 03/031588 A2

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

TITLE OF THE INVENTION
HEPATITIS C VIRUS VACCINE

RELATED APPLICATIONS

The present application claims priority to provisional applications U.S. Serial No. 60/363,774, filed March 13, 2002, and U.S. Serial No. 60/328,655, filed October 11, 2001, each of which are hereby incorporated by reference herein.

BACKGROUND OF THE INVENTION

The references cited in the present application are not admitted to be prior art to the claimed invention.

About 3% of the world's population are infected with the Hepatitis C virus (HCV). (Wasley *et al.*, *Semin. Liver Dis. 20*, 1-16, 2000.) Exposure to HCV results in an overt acute disease in a small percentage of cases, while in most instances the virus establishes a chronic infection causing liver inflammation and slowly progresses into liver failure and cirrhosis. (Iwarson, *FEMS Microbiol. Rev. 14*, 201-204, 1994.) In addition, epidemiological surveys indicate an important role of HCV in the pathogenesis of hepatocellular carcinoma. (Kew, *FEMS Microbiol. Rev. 14*, 211-220, 1994, Alter, *Blood 85*, 1681-1695, 1995.)

Prior to the implementation of routine blood screening for HCV in 1992, most infections were contracted by inadvertent exposure to contaminated blood, blood products or transplanted organs. In those areas where blood screening of HCV is carried out, HCV is primarily contracted through direct percutaneous exposure to infected blood, *i.e.*, intravenous drug use. Less frequent methods of transmission include perinatal exposure, hemodialysis, and sexual contact with an HCV infected person. (Alter *et al.*, *N. Engl. J. Med. 341(8)*, 556-562, 1999, Alter, *J. Hepatol. 31 Suppl.* 88-91, 1999. *Semin. Liver. Dis. 201*, 1-16, 2000.)

The HCV genome consists of a single strand RNA about 9.5 kb encoding a precursor polyprotein of about 3000 amino acids. (Choo *et al.*, *Science 244*, 362-364, 1989, Choo *et al.*, *Science 244*, 359-362, 1989, Takamizawa *et al.*, *J. Virol. 65*, 1105-1113, 1991.) The HCV polyprotein contains the viral proteins in the order: C-E1-E2-p7-NS2-NS3-NS4A-NS4B-NS5A-NS5B.

Individual viral proteins are produced by proteolysis of the HCV polyprotein. Host cell proteases release the putative structural proteins C, E1, E2, and

p7, and create the N-terminus of NS2 at amino acid 810. (Mizushima *et al., J. Virol. 68*, 2731-2734, 1994, Hijikata *et al., P.N.A.S. USA 90*, 10773-10777, 1993.)

The non-structural proteins NS3, NS4A, NS4B, NS5A and NS5B presumably form the virus replication machinery and are released from the polyprotein. A zinc-dependent protease associated with NS2 and the N-terminus of NS3 is responsible for cleavage between NS2 and NS3. (Grakoui *et al., J. Virol. 67*, 1385-1395, 1993, Hijikata *et al., P.N.A.S. USA 90*, 10773-10777, 1993.) A distinct serine protease located in the N-terminal domain of NS3 is responsible for proteolytic cleavages at the NS3/NS4A, NS4A/NS4B, NS4B/NS5A and NS5A/NS5B junctions. (Bartenschlager *et al., J. Virol. 67*, 3835-3844, 1993, Grakoui *et al., Proc. Natl. Acad. Sci. USA 90*, 10583-10587, 1993, Tomei *et al., J. Virol. 67*, 4017-4026, 1993.) NS4A provides a cofactor for NS3 activity. (Failla *et al., J. Virol. 68*, 3753-3760, 1994, De Francesco *et al.*, U.S. Patent No. 5,739,002.)

NS5A is a highly phosphorylated protein conferring interferon resistance. (De Francesco *et al., Semin. Liver Dis., 20*(1), 69-83, 2000, Pawlotsky, *Viral Hepat. Suppl. 1*, 47-48, 1999.)

NS5B provides an RNA-dependent RNA polymerase. (De Francesco *et al.*, International Publication Number WO 96/37619, Behrens *et al., EMBO 15*, 12-22, 1996, Lohmann *et al., Virology 249*, 108-118, 1998.)

SUMMARY OF THE INVENTION

The present invention features Ad6 vectors and a nucleic acid encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide containing an inactive NS5B RNA-dependent RNA polymerase region. The nucleic acid is particularly useful as a component of an adenovector or DNA plasmid vaccine providing a broad range of antigens for generating an HCV specific cell mediated immune (CMI) response against HCV.

A HCV specific CMI response refers to the production of cytotoxic T lymphocytes and T helper cells that recognize an HCV antigen. The CMI response may also include non-HCV specific immune effects.

Preferred nucleic acids encode a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide that is substantially similar to SEQ. ID. NO. 1 and has sufficient protease activity to process itself to produce at least a polypeptide substantially similar to the NS5B region present in SEQ. ID. NO. 1. The produced polypeptide corresponding to NS5B is enzymatically inactive. More preferably, the HCV polypeptide has sufficient

protease activity to produce polypeptides substantially similar to the NS3, NS4A, NS4B, NS5A, and NS5B regions present in SEQ. ID. NO. 1.

Reference to a "substantially similar sequence" indicates an identity of at least about 65% to a reference sequence. Thus, for example, polypeptides having an amino acid sequence substantially similar to SEQ. ID. NO. 1 have an overall amino acid identity of at least about 65% to SEQ. ID. NO. 1.

Polypeptides corresponding to NS3, NS4A, NS4B, NS5A, and NS5B have an amino acid sequence identity of at least about 65% to the corresponding region in SEQ. ID. NO. 1. Such corresponding polypeptides are also referred to herein as NS3, NS4A, NS4B, NS5A, and NS5B polypeptides.

Thus, a first aspect of the present invention describes a nucleic acid comprising a nucleotide sequence encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide substantially similar to SEQ. ID. NO. 1. The encoded polypeptide has sufficient protease activity to process itself to produce an NS5B polypeptide that is enzymatically inactive.

In a preferred embodiment, the nucleic acid is an expression vector capable of expressing the Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide in a desired human cell. Expression inside a human cell has therapeutic applications for actively treating an HCV infection and for prophylactically treating against an HCV infection.

An expression vector contains a nucleotide sequence encoding a polypeptide along with regulatory elements for proper transcription and processing. The regulatory elements that may be present include those naturally associated with the nucleotide sequence encoding the polypeptide and exogenous regulatory elements not naturally associated with the nucleotide sequence. Exogenous regulatory elements such as an exogenous promoter can be useful for expression in a particular host, such as in a human cell. Examples of regulatory elements useful for functional expression include a promoter, a terminator, a ribosome binding site, and a polyadenylation signal.

Another aspect of the present invention describes a nucleic acid comprising a gene expression cassette able to express in a human cell a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide substantially similar to SEQ. ID. NO. 1. The polypeptide can process itself to produce an enzymatically inactive NS5B protein. The gene expression cassette contains at least the following:

a) a promoter transcriptionally coupled to a nucleotide sequence encoding a polypeptide;

b) a 5' ribosome binding site functionally coupled to the nucleotide sequence,

c) a terminator joined to the 3' end of the nucleotide sequence, and

d) a 3' polyadenylation signal functionally coupled to the nucleotide sequence.

Reference to "transcriptionally coupled" indicates that the promoter is positioned such that transcription of the nucleotide sequence can be brought about by RNA polymerase binding at the promoter. Transcriptionally coupled does not require that the sequence being transcribed is adjacent to the promoter.

Reference to "functionally coupled" indicates the ability to mediate an effect on the nucleotide sequence. Functionally coupled does not require that the coupled sequences be adjacent to each other. A 3' polyadenylation signal functionally coupled to the nucleotide sequence facilitates cleavage and polyadenylation of the transcribed RNA. A 5' ribosome binding site functionally coupled to the nucleotide sequence facilitates ribosome binding.

In preferred embodiments the nucleic acid is a DNA plasmid vector or an adenovector suitable for either therapeutic application in treating HCV or as an intermediate in the production of a therapeutic vector. Treating HCV includes actively treating an HCV infection and prophylactically treating against an HCV infection.

Another aspect of the present invention describes an adenovector comprising a Met-NS3-NS4A-NS4B-NS5A-NS5B expression cassette able to express a polypeptide substantially similar to SEQ. ID. NO. 1 that is produced by a process involving (a) homologous recombination and (b) adenovector rescue. The homologous recombinant step produces an adenovirus genome plasmid. The adenovector rescue step produces the adenovector from the adenogenome plasmid.

Adenovirus genome plasmids described herein contain a recombinant adenovirus genome having a deletion in the E1 region and optionally in the E3 region and a gene expression cassette inserted into one of the deleted regions. The recombinant adenovirus genome is made of regions substantially similar to one or more adenovirus serotypes.

Another aspect of the present invention describes an adenovector consisting of the nucleic acid sequence of SEQ. ID. NO. 4 or a derivative thereof,

wherein said derivative thereof has the HCV polyprotein encoding sequence present in SEQ. ID. NO. 4 replaced with the HCV polyprotein encoding sequence of either SEQ. ID. NO. 3, SEQ. ID. NO. 10 or SEQ. ID. NO. 11.

Another aspect of the present invention describes a cultured recombinant cell comprising a nucleic acid containing a sequence encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide substantially similar to SEQ. ID. NO. 1. The recombinant cell has a variety of uses such as being used to replicate nucleic acid encoding the polypeptide in vector construction methods.

Another aspect of the present invention describes a method of making an adenovector comprising a Met-NS3-NS4A-NS4B-NS5A-NS5B expression cassette able to express a polypeptide substantially similar to SEQ. ID. NO. 1. The method involves the steps of (a) producing an adenovirus genome plasmid containing a recombinant adenovirus genome with deletions in the E1 and E3 regions and a gene expression cassette inserted into one of the deleted regions and (b) rescuing the adenovector from the adenovirus genome plasmid.

Another aspect of the present invention describes a pharmaceutical composition comprising a vector for expressing a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide substantially similar to SEQ. ID. NO. 1 and a pharmaceutically acceptable carrier. The vector is suitable for administration and polypeptide expression in a patient.

A "patient" refers to a mammal capable of being infected with HCV. A patient may or may not be infected with HCV. Examples of patients are humans and chimpanzees.

Another aspect of the present invention describes a method of treating a patient comprising the step of administering to the patient an effective amount of a vector expressing a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide substantially similar to SEQ. ID. NO. 1. The vector is suitable for administration and polypeptide expression in the patient.

The patient undergoing treatment may or may not be infected with HCV. For a patient infected with HCV, an effective amount is sufficient to achieve one or more of the following effects: reduce the ability of HCV to replicate, reduce HCV load, increase viral clearance, and increase one or more HCV specific CMI responses. For a patient not infected with HCV, an effective amount is sufficient to achieve one or more of the following: an increased ability to produce one or more components of a HCV specific CMI response to a HCV infection, a reduced

susceptibility to HCV infection, and a reduced ability of the infecting virus to establish persistent infection for chronic disease.

Another aspect of the present invention features a recombinant nucleic acid comprising an Ad6 region and a region not present in Ad6. Reference to "recombinant" nucleic acid indicates the presence of two or more nucleic acid regions not naturally associated with each other. Preferably, the Ad6 recombinant nucleic acid contains Ad6 regions and a gene expression cassette coding for a polypeptide heterologous to Ad6.

Other features and advantages of the present invention are apparent from the additional descriptions provided herein including the different examples. The provided examples illustrate different components and methodology useful in practicing the present invention. The examples do not limit the claimed invention. Based on the present disclosure the skilled artisan can identify and employ other components and methodology useful for practicing the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A and 1B illustrate SEQ. ID. NO. 1.

Figures 2A, 2B, 2C, and 2D illustrate SEQ. ID. NO. 2. SEQ. ID. NO. 2 provides a nucleotide sequence coding for SEQ. ID. NO. 1 along with an optimized internal ribosome entry site and TAAA termination. Nucleotides 1-6 provides an optimized internal ribosome entry site. Nucleotides 7-5961 code for a HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide with nucleotides in positions 5137 to 5145 providing a AlaAlaGly sequence in amino acid positions 1711 to 1713 that renders NS5B inactive. Nucleotides 5962-5965 provide a TAAA termination.

Figures 3A, 3B, 3C, and 3D illustrate SEQ. ID. NO. 3. SEQ. ID. NO. 3 is a codon optimized version of SEQ. ID. NO. 2. Nucleotides 7-5961 encode a HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide.

Figures 4A-4M illustrate MRKAd6-NSmut (SEQ. ID. NO. 4). SEQ. ID. NO. 4 is an adenovector containing an expression cassette where the polypeptide of SEQ. ID. NO. 1 is encoded by SEQ. ID. NO. 2. Base pairs 1-450 correspond to the Ad5 bp 1 to 450; base pairs 462 to 1252 correspond to the human CMV promoter; base pairs 1258 to 1267 correspond to the Kozak sequence; base pairs 1264 to 7222 correspond to the NS genes; base pairs 7231 to 7451 correspond to the BGH polyadenylation signal; base pairs 7469 to 9506 correspond to Ad5 base pairs 3511 to 5548; base pairs 9507 to 32121 correspond to Ad6 base pairs 5542 to 28156; base

pairs 32122 to 35117 correspond to Ad6 base pairs 30789 to 33784; and base pairs 35118 to 37089 correspond to Ad5 base pairs 33967 to 35935.

Figures 5A-5O illustrate SEQ. ID. NOs. 5 and 6. SEQ. ID. NO. 5 encodes a HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide with an active RNA dependent RNA polymerase. SEQ. ID. NO. 6 provides the amino acid sequence for the polypeptide.

Figures 6A-6C provide the nucleic acid sequence for pV1JnsA (SEQ. ID. NO. 7).

Figures 7A-7N provide the nucleic acid sequence for the Ad6 genome (SEQ. ID. NO. 8).

Figures 8A-8K provide the nucleic acid sequence for the Ad5 genome (SEQ. ID. NO. 9).

Figure 9 illustrates different regions of the Ad6 genome. The linear (35759 bp) ds DNA genome is indicated by two parallel lines and is divided into 100 map units. Transcription units are shown relative to their position and orientation in the genome. Early genes (E1A, E1B, E2A/B, E3 and E4 are indicated by gray arrows. Late genes (L1 to L5) , indicated by black arrows, are produced by alternative splicing of a transcript produced from the major late promoter (MLP) and all contain the tripartite leader (1, 2, 3) at their 5' ends. The E1 region is located from approximately 1.0 to 11.5 map units, the E2 region from 75.0 to 11.5 map units, E3 from 76.1 to 86.7 map units, and E4 from 99.5 to 91.2 map units. The major late transcription unit is located between 16.0 and 91.2 map units.

Figure 10 illustrates homologous recombination to recover pAdE1-E3+ containing Ad6 and Ad5 regions.

Figure 11 illustrates homologous recombinant to recover a pAdE1-E3+ containing Ad6 regions.

Figure 12 illustrates a western blot on whole-cell extracts from 293 cells transfected with plasmid DNA expressing different HCV NS cassettes. Mature NS3 and NS5A products were detected with specific antibodies. "pV1Jns-NS" refers to a pV1JnsA plasmid where a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide is encoded by SEQ. ID. NO. 5, and SEQ. ID. NO. 5 is inserted between bases 1881 and 1912 of SEQ. ID. NO. 7. "pV1Jns-NSmut" refers to a pV1JnsA plasmid where SEQ. ID. NO. 2 is inserted between bases 1882 and 1925 of SEQ. ID. NO. 7. "pV1Jns-NSOPTmut" refers to a pV1JnsA plasmid where SEQ. ID. NO. 3 is inserted between bases 1881 and 1905 of SEQ. ID. NO. 7.

Figures 13A and 13B illustrate T cell responses by IFNγ ELIspot induced in C57black6 mice (A) and BalbC mice (B) by two injections of 25μg and 50μg, respectively, of plasmid DNA encoding the different HCV NS cassettes with Gene Electro-Transfer (GET).

Figure 14 illustrates protein expression from different adenovectors upon infection of HeLa cells. MRKAd5-NSmut is an adenovector based on an Ad5 sequence (SEQ. ID. NO. 9), where the Ad5 genome has an E1 deletion of base pairs 451 to 3510, an E3 deletion of base pairs 28134 to 30817, and has the NS3-NS4A-NS4B-NS5A-NS5B expression cassette as provided in base pairs 451 to 7468 of SEQ. ID. NO. 4 inserted between positions 450 and 3511. Ad5-NS is an adenovector based on an Ad5 backbone with an E1 deletion of base pairs 342 to 3523, and E3 deletion of base pairs 28134 to 30817 and containing an expression cassette encoding a NS3-NS4A-NS4B-NS5A-NS5B from SEQ. ID. NO. 5. "MRKAd6-NSOPTmut" refers to an adenovector having a modified SEQ. ID. NO. 4 sequence, wherein base pairs 1258 to 7222 of SEQ. ID. NO. 4 is replaced with SEQ. ID. NO. 3.

Figure 15 illustrates T cell responses by IFNγ ELIspot induced in C57black6 mice by two injections of 10^9 vp of adenovectors containing different HCV non-structural gene cassettes.

Figures 16A-16D illustrate T cell responses by IFNγ ELIspot induced in Rhesus monkeys by one or two injections of 10^{10} vp (A) or 10^{11} vp (B) of adenovectors containing different HCV non-structural gene cassettes.

Figures 17A and 17B illustrates CD8+ T cell responses by IFNγ ICS induced in Rhesus monkeys by two injections of 10^{10} vp (A) or 10^{11} vp (B) of adenovectors encoding the different HCV non-structural gene cassettes.

Figures 18A-18F illustrate T cell responses by bulk CTL assay induced in Rhesus monkeys by two injections of 10^{11} vp of Ad5-NS (A), MRKAd5-NSmut (B), or MRKAd6-NSmut (C).

Figure 19 illustrates the plasmid pE2.

Figures 20A-D illustrates the partial codon optimized sequence NSsuboptmut (SEQ. ID. NO. 10). Coding sequence for the Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide is from base 7 to 5961.

DETAILED DESCRIPTION OF THE INVENTION

The present invention features Ad6 vectors and nucleic acid encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide that contains an inactive NS5B region. Providing an inactive NS5B region supplies NS5B antigens while reducing the possibility of adverse side effects due to an active viral RNA polymerase. Uses of the featured nucleic acid include use as a vaccine component to introduce into a cell an HCV polypeptide that provides a broad range of antigens for generating a CMI response against HCV, and as an intermediate for producing such a vaccine component.

The adaptive cellular immune response can function to recognize viral antigens in HCV infected cells throughout the body due to the ubiquitous distribution of major histocompatibility complex (MHC) class I and II expression, to induce immunological memory, and to maintain immunological memory. These functions are attributed to antigen-specific CD4+ T helper (Th) and CD8+ cytotoxic T cells (CTL).

Upon activation via their specific T cell receptors, HCV specific Th cells fulfill a variety of immunoregulatory functions, most of them mediated by Th1 and Th2 cytokines. HCV specific Th cells assist in the activation and differentiation of B cells and induction and stimulation of virus-specific cytotoxic T cells. Together with CTL, Th cells may also secrete IFN-γ and TNF-α that inhibit replication and gene expression of several viruses. Additionally, Th cells and CTL, the main effector cells, can induce apoptosis and lysis of virus infected cells.

HCV specific CTL are generated from antigens processed by professional antigen presenting cells (pAPCs). Antigens can be either synthesized within or introduced into pAPCs. Antigen synthesis in a pAPC can be brought about by introducing into the cell an expression cassette encoding the antigen.

A preferred route of nucleic acid vaccine administration is an intramuscular route. Intramuscular administration appears to result in the introduction and expression of nucleic acid into somatic cells and pAPCs. HCV antigens produced in the somatic cells can be transferred to pAPCs for presentation in the context of MHC class I molecules. (Donnelly *et al.*, *Annu. Rev. Immunol. 15*:617-648, 1997.)

pAPCs process longer length antigens into smaller peptide antigens in the proteasome complex. The antigen is translocated into the endoplasmic reticulum/Golgi complex secretory pathway for association with MHC class I

proteins. CD8+ T lymphocytes recognize antigen associated with class I MHC via the T cell receptor (TCR) and the CD8 cell surface protein.

Using a nucleic acid encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide as a vaccine component allows for production of a broad range of antigens capable of generating CMI responses from a single vector. The polypeptide should be able to process itself sufficiently to produce at least a region corresponding to NS5B. Preferred nucleic acids encode an amino acid sequence substantially similar to SEQ. ID. NO. 1 that has sufficient protease activity to process itself to produce individual HCV polypeptides substantially similar to the NS3, NS4A, NS4B, NS5A, and NS5B regions present in SEQ. ID. NO. 1.

A polypeptide substantially similar to SEQ. ID. NO. 1 with sufficient protease activity to process itself in a cell provides the cell with T cell epitopes that are present in several different HCV strains. Protease activity is provided by NS3 and NS3/NS4A proteins digesting the Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide at the appropriate cleavage sites to release polypeptides corresponding to NS3, NS4A, NS4B, NS5A, and NS5B. Self- processing of the Met-NS3-NS4A-NS4B-NS5A-NS5B generates polypeptides that approximate naturally occurring HCV polypeptides.

Based on the guidance provided herein a sufficiently strong immune response can be generated to achieve beneficial effects in a patient. The provided guidance includes information concerning HCV sequence selection, vector selection, vector production, combination treatment, and administration.

I. HCV SEQUENCES

A variety of different nucleic acid sequences can be used as a vaccine component to supply a HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide to a cell or as an intermediate to produce vaccine components. The starting point for obtaining suitable nucleic acid sequences are preferably naturally occurring NS3-NS4A-NS4B-NS5A-NS5B polypeptide sequences modified to produce an inactive NS5B.

The use of a HCV nucleic acid sequence providing HCV non-structural antigens to generate a CMI response is mentioned by Cho *et al., Vaccine 17*:1136-1144, 1999, Paliard *et al.*, International Publication Number WO 01/30812 (not admitted to be prior art to the claimed invention), and Coit *et al.*, International Publication Number WO 01/38360 (not admitted to be prior art to the claimed invention). Such references fail to describe, for example, a polypeptide that processes

itself to produce an inactive NS5B, and the particular combinations of HCV sequences and delivery vehicles employed herein.

Modifications to a HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide sequence can be produced by altering the encoding nucleic acid. Alterations can be performed to create deletions, insertions and substitutions.

Small modifications can be made in NS5B to produce an inactive polymerase by targeting motifs essentially for replication. Examples of motifs critical for NS5B activity and modifications that can be made to produce an inactive NS5B are described by Lohmann *et al., Journal of Virology 71*:8416-8426, 1997, and Kolykhalov *et al., Journal of Virology 74*:2046-2051, 2000.

Additional factors to take into account when producing modifications to a HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide include maintaining the ability to self-process and maintaining T cell antigens. The ability of the HCV polypeptide to process itself is determined to a large extent by a functional NS3 protease. Modifications that maintain NS3 activity protease activity can be obtained by taking into account the NS3 protein, NS4A which serves as a cofactor for NS3, and NS3 protease recognition sites present within the NS3-NS4A-NS4B-NS5A-NS5B polypeptide.

Different modifications can be made to naturally occurring NS3-NS4A-NS4B-NS5A-NS5B polypeptide sequences to produce polypeptides able to elicit a broad range of T cell responses. Factors influencing the ability of a polypeptide to elicit a broad T cell response include the preservation or introduction of HCV specific T cell antigen regions and prevalence of different T cell antigen regions in different HCV isolates.

Numerous examples of naturally occurring HCV isolates are well known in the art. HCV isolates can be classified into the following six major genotypes comprising one or more subtypes: HCV-1/(1a,1b,1c), HCV-2/(2a,2b,2c), HCV-3/(3a,3b,10a), HCV-4/(4a), HCV-5/(5a) and HCV-6/(6a,6b,7b,8b,9a,11a). (Simmonds, *J. Gen. Virol.,* 693-712, 2001.) Examples of particular HCV sequences such as HCV-BK, HCV-J, HCV-N, HCV-H, have been deposited in GenBank and described in various publications. (See, for example, Chamberlain *et al., J. Gen. Virol.,* 1341-1347, 1997.)

HCV T cell antigens can be identified by, for example, empirical experimentation. One way of identifying T cell antigens involves generating a series of overlapping short peptides from a longer length polypeptide and then screening the

T-cell populations from infected patients for positive clones. Positive clones are activated/primed by a particular peptide. Techniques such as IFNγ-ELISPOT, IFNγ-Intracellular staining and bulk CTL assays can be used to measure peptide activity. Peptides thus identified can be considered to represent T-cell epitopes of the respective pathogen.

HCV T cell antigen regions from different HCV isolates can be introduced into a single sequence by, for example, producing a hybrid NS3-NS4A-NS4B-NS5A-NS5B polypeptide containing regions from two or more naturally occurring sequences. Such a hybrid can contain additional modifications, which preferably do not reduce the ability of the polypeptide to produce an HCV CMI response.

The ability of a modified Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide to process itself and produce a CMI response can be determined using techniques described herein or well known in the art. Such techniques include the use of IFNγ-ELISPOT, IFNγ-Intracellular staining and bulk CTL assays to measure a HCV specific CMI response.

A. Met-NS3-NS4A-NS4B-NS5A-NS5B Sequences

SEQ. ID. NO. 1 provides a preferred Met-NS3-NS4A-NS4B-NS5A-NS5B sequence. SEQ. ID. NO. 1 contains a large number of HCV specific T cell antigens that are present in several different HCV isolates. SEQ. ID. NO. 1 is similar to the NS3-NS4A-NS4B-NS5A-NS5B portion of the HCV BK strain nucleotide sequence (GenBank accession number M58335).

In SEQ. ID. NO. 1 anchor positions important for recognition by MHC class I molecules are conserved or represent conservative substitutions for 18 out of 20 known T-cell epitopes in the NS3-NS4A-NS4B-NS5A-NS5B portion of HCV polyproteins. With respect to the remaining two known T-cell epitopes, one has a non-conservative anchor substitution in SEQ. ID. NO. 1 that may still be recognized by a different HLA supertype and one epitope has one anchor residue not conserved. HCV T-cell epitopes are described in Chisari *et al., Curr. Top. Microbiol Immunol., 242*:299-325, 2000, and Lechner et al. *J. Exp. Med. 9*:1499-1512, 2000.

Differences between the HCV-BK NS3-NS4A-NS4B-NS5A-NS5B nucleotide sequence and SEQ. ID. NO. 1 include the introduction of a methionine at the 5' end and the presence of modified NS5B active site residues in SEQ. ID. NO. 1.

The modification replaces GlyAspAsp with AlaAlaGly (residues 1711-1713) to inactivate NS5B.

The encoded HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide preferably has an amino acid sequence substantially similar to SEQ. ID. NO. 1. In different embodiments, the encoded HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide has an amino acid identify to SEQ. ID. NO. 1 of at least 65%, at least 75%, at least 85%, at least 95%, at least 99% or 100%; or differs from SEQ. ID. NO. 1 by 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 1-11, 1-12, 1-13, 1-14, 1-15, 1-16, 1-17, 1-18, 1-19, or 1-20 amino acids.

Amino acid differences between a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide and SEQ. ID. NO. 1 are calculated by determining the minimum number of amino acid modifications in which the two sequences differ. Amino acid modifications can be deletions, additions, substitutions or any combination thereof.

Amino acid sequence identity is determined by methods well known in the art that compare the amino acid sequence of one polypeptide to the amino acid sequence of a second polypeptide and generate a sequence alignment. Amino acid identity is calculated from the alignment by counting the number of aligned residue pairs that have identical amino acids.

Methods for determining sequence identity include those described by Schuler, G.D. in *Bioinformatics: A Practical Guide to the Analysis of Genes and Proteins*, Baxevanis, A.D. and Ouelette, B.F.F., eds., John Wiley & Sons, Inc, 2001; Yona, *et al.*, in *Bioinformatics: Sequence, structure and databanks*, Higgins, D. and Taylor, W. eds, Oxford University Press, 2000; and *Bioinformatics: Sequence and Genome Analysis*, Mount, D.W., ed., Cold Spring Harbor Laboratory Press, 2001). Methods to determine amino acid sequence identity are codified in publicly available computer programs such as GAP (Wisconsin Package Version 10.2, Genetics Computer Group (GCG), Madison, Wisc.), BLAST (Altschul *et al.*, *J. Mol. Biol. 215(3)*:403-10, 1990), and FASTA (Pearson, *Methods in Enzymology 183*:63-98, 1990, R.F. Doolittle, ed.).

In an embodiment of the present invention sequence identity between two polypeptides is determined using the GAP program (Wisconsin Package Version 10.2, Genetics Computer Group (GCG), Madison, Wisc.). GAP uses the alignment method of Needleman and Wunsch. (Needleman, *et al.*, *J. Mol. Biol. 48*:443-453, 1970.) GAP considers all possible alignments and gap positions between two sequences and creates a global alignment that maximizes the number of matched

residues and minimizes the number and size of gaps. A scoring matrix is used to assign values for symbol matches. In addition, a gap creation penalty and a gap extension penalty are required to limit the insertion of gaps into the alignment. Default program parameters for polypeptide comparisons using GAP are the BLOSUM62 (Henikoff *et al., Proc. Natl. Acad. Sci. USA, 89*:10915-10919, 1992) amino acid scoring matrix (MATrix=blosum62.cmp), a gap creation parameter (GAPweight=8) and a gap extension pararameter (LENgthweight=2).

More preferred HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptides in addition to being substantially similar to SEQ. ID. NO. 1 across their entire length produce individual NS3, NS4A, NS4B, NS5A and NS5B regions that are substantially similar to the corresponding regions present in SEQ. ID. NO. 1. The corresponding regions in SEQ. ID. NO. 1 are provided as follows: Met-NS3 amino acids 1-632; NS4A amino acids 633-686; NS4B amino acids 687-947; NS5A amino acids 948-1394; and NS5B amino acids 1395-1985.

In different embodiments a NS3, NS4A, NS4B, NS5A and/or NS5B region has an amino acid identity to the corresponding region in SEQ. ID. NO. 1 of at least 65%, at least 75%, at least 85%, at least 95%, at least 99%, or 100%; or an amino acid difference of 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 1-11, 1-12, 1-13, 1-14, 1-15, 1-16, 1-17, 1-18, 1-19, or 1-20 amino acids.

Amino acid modifications to SEQ. ID. NO. 1 preferably maintain all or most of the T-cell antigen regions. Differences in naturally occurring amino acids are due to different amino acid side chains (R groups). An R group affects different properties of the amino acid such as physical size, charge, and hydrophobicity. Amino acids can be divided into different groups as follows: neutral and hydrophobic (alanine, valine, leucine, isoleucine, proline, tyrptophan, phenylalanine, and methionine); neutral and polar (glycine, serine, threonine, tryosine, cysteine, asparagine, and glutamine); basic (lysine, arginine, and histidine); and acidic (aspartic acid and glutamic acid).

Generally, in substituting different amino acids it is preferable to exchange amino acids having similar properties. Substituting different amino acids within a particular group, such as substituting valine for leucine, arginine for lysine, and asparagine for glutamine are good candidates for not causing a change in polypeptide tertiary structure.

Starting with a particular amino acid sequence and the known degeneracy of the genetic code, a large number of different encoding nucleic acid

sequences can be obtained. The degeneracy of the genetic code arises because almost all amino acids are encoded by different combinations of nucleotide triplets or "codons". The translation of a particular codon into a particular amino acid is well known in the art (*see, e.g.*, Lewin *GENES IV*, p. 119, Oxford University Press, 1990). Amino acids are encoded by codons as follows:

A=Ala=Alanine: codons GCA, GCC, GCG, GCU
C=Cys=Cysteine: codons UGC, UGU
D=Asp=Aspartic acid: codons GAC, GAU
E=Glu=Glutamic acid: codons GAA, GAG
F=Phe=Phenylalanine: codons UUC, UUU
G=Gly=Glycine: codons GGA, GGC, GGG, GGU
H=His=Histidine: codons CAC, CAU
I=Ile=Isoleucine: codons AUA, AUC, AUU
K=Lys=Lysine: codons AAA, AAG
L=Leu=Leucine: codons UUA, UUG, CUA, CUC, CUG, CUU
M=Met=Methionine: codon AUG
N=Asn=Asparagine: codons AAC, AAU
P=Pro=Proline: codons CCA, CCC, CCG, CCU
Q=Gln=Glutamine: codons CAA, CAG
R=Arg=Arginine: codons AGA, AGG, CGA, CGC, CGG, CGU
S=Ser=Serine: codons AGC, AGU, UCA, UCC, UCG, UCU
T=Thr=Threonine: codons ACA, ACC, ACG, ACU
V=Val=Valine: codons GUA, GUC, GUG, GUU
W=Trp=Tryptophan: codon UGG
Y=Tyr=Tyrosine: codons UAC, UAU.

Nucleic acid sequences can be optimized in an effort to enhance expression in a host. Factors to be considered include C:G content, preferred codons, and the avoidance of inhibitory secondary structure. These factors can be combined in different ways in an attempt to obtain nucleic acid sequences having enhanced expression in a particular host. (See, for example, Donnelly *et al.*, International Publication Number WO 97/47358.)

The ability of a particular sequence to have enhanced expression in a particular host involves some empirical experimentation. Such experimentation involves measuring expression of a prospective nucleic acid sequence and, if needed, altering the sequence.

B. Encoding Nucleotide Sequences

SEQ. ID. NOs. 2 and 3 provide two examples of nucleotide sequences encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B sequence. The coding sequence of SEQ. ID. NO. 2 is similar (99.4% nucleotide sequence identity) to the NS3-NS4A-NS4B-NS5A-NS5B region of the naturally occurring HCV-BK sequence (GenBank accession number M58335). SEQ. ID. NO. 3 is a codon-optimized version of SEQ. ID. NO. 2. SEQ. ID. NOs. 2 and 3 have a nucleotide sequence identity of 78.3%.

Differences between the HCV-BK NS3-NS4A-NS4B-NS5A-NS5B nucleotide (GenBank accession number M58335) and SEQ. ID. NO. 2, include SEQ. ID. NO. 2 having a ribosome binding site, an ATG methionine codon, a region coding for a modified NS5B catalytic domain, a TAAA stop signal and an additional 30 nucleotide differences. The modified catalytic domain codes for a AlaAlaGly (residues 1711-1713) instead of GlyAspAsp to inactivate NS5B.

A nucleotide sequence encoding a HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide is preferably substantially similar to the SEQ. ID. NO. 2 coding region. In different embodiments, the nucleotide sequence encoding a HCV Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide has a nucleotide sequence identify to the SEQ. ID. NO. 2 coding region of at least 65%, at least 75%, at least 85%, at least 95%, at least 99%, or 100%; or differs from SEQ. ID. NO. 2 by 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 1-11, 1-12, 1-13, 1-14, 1-15, 1-16, 1-17, 1-18, 1-19, 1-20, 1-25, 1-30, 1-35, 1-40, 1-45, or 1-50 nucleotides.

Nucleotide differences between a sequence coding Met-NS3-NS4A-NS4B-NS5A-NS5B and the SEQ. ID. NO. 2 coding region are calculated by determining the minimum number of nucleotide modifications in which the two sequences differ. Nucleotide modifications can be deletions, additions, substitutions or any combination thereof.

Nucleotide sequence identity is determined by methods well known in the art that compare the nucleotide sequence of one sequence to the nucleotide sequence of a second sequence and generate a sequence alignment. Sequence identity is determined from the alignment by counting the number of aligned positions having identical nucleotides.

Methods for determining nucleotide sequence identity between two polynucleotides include those described by Schuler, in *Bioinformatics: A Practical Guide to the Analysis of Genes and Proteins*, Baxevanis, A.D. and Ouelette, B.F.F.,

eds., John Wiley & Sons, Inc, 2001; Yona *et al.,*. in *Bioinformatics: Sequence, structure and databanks*, Higgins, D. and Taylor, W. eds, Oxford University Press, 2000; and *Bioinformatics: Sequence and Genome Analysis*, Mount, D.W., ed., Cold Spring Harbor Laboratory Press, 2001). Methods to determine nucleotide sequence identity are codified in publicly available computer programs such as GAP (Wisconsin Package Version 10.2, Genetics Computer Group (GCG), Madison, Wisc.), BLAST (Altschul *et al., J. Mol. Biol. 215(3)*:403-10, 1990), and FASTA (Pearson, W.R., *Methods in Enzymology 183*:63-98, 1990, R.F. Doolittle, ed.).

In an embodiment of the present ivnention, sequence identity between two polynucleotides is determined by application of GAP (Wisconsin Package Version 10.2, Genetics Computer Group (GCG), Madison, Wisc.). GAP uses the alignment method of Needleman and Wunsch. (Needleman *et al., J. Mol. Biol. 48*:443-453, 1970.) GAP considers all possible alignments and gap positions between two sequences and creates a global alignment that maximizes the number of matched residues and minimizes the number and size of gaps. A scoring matrix is used to assign values for symbol matches. In addition, a gap creation penalty and a gap extension penalty are required to limit the insertion of gaps into the alignment. Default program parameters for polynucleotide comparisons using GAP are the nwsgapdna.cmp scoring matrix (MATrix=nwsgapdna.cmp), a gap creation parameter (GAPweight=50) and a gap extension pararameter (LENgthweight=3).

More preferred HCV Met-NS3-NS4A-NS4B-NS5A-NS5B nucleotide sequences in addition to being substantially similar across its entire length, produce individual NS3, NS4A, NS4B, NS5A and NS5B regions that are substantially similar to the corresponding regions present in SEQ. ID. NO. 2. The corresponding coding regions in SEQ. ID. NO. 2 are provided as follows: Met-NS3, nucleotides 7-1902; NS4A nucleotides 1903-2064; NS4B nucleotides 2065-2847; NS5A nucleotides 2848-4188: NS5B nucleotides 4189-5661.

In different embodiments a NS3, NS4A, NS4B, NS5A and/or NS5B encoding region has a nucleotide sequence identity to the corresponding region in SEQ. ID. NO. 2 of at least 65%, at least 75%, at least 85%, at least 95%, at least 99% or 100%; or a nucleotide difference to SEQ. ID. NO. 2 of 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 1-11, 1-12, 1-13, 1-14, 1-15, 1-16, 1-17, 1-18, 1-19, 1-20, 1-25, 1-30, 1-35, 1-40, 1-45, or 1-50 nucleotides.

C. Gene Expression Cassettes

A gene expression cassette contains elements needed for polypeptide expression. Reference to "polypeptide" does not provide a size limitation and includes protein. Regulatory elements present in a gene expression cassette generally include: (a) a promoter transcriptionally coupled to a nucleotide sequence encoding the polypeptide, (b) a 5' ribosome binding site functionally coupled to the nucleotide sequence, (c) a terminator joined to the 3' end of the nucleotide sequence, and (d) a 3' polyadenylation signal functionally coupled to the nucleotide sequence. Additional regulatory elements useful for enhancing or regulating gene expression or polypeptide processing may also be present.

Promoters are genetic elements that are recognized by an RNA polymerase and mediate transcription of downstream regions. Preferred promoters are strong promoters that provide for increased levels of transcription. Examples of strong promoters are the immediate early human cytomegalovirus promoter (CMV), and CMV with intron A. (Chapman *et al, Nucl. Acids Res.* 19:3979-3986, 1991.) Additional examples of promoters include naturally occurring promoters such as the EF1 alpha promoter, the murine CMV promoter, Rous sarcoma virus promoter, and SV40 early/late promoters and the β-actin promoter; and artificial promoters such as a synthetic muscle specific promoter and a chimeric muscle-specific/CMV promoter (Li *et al., Nat. Biotechnol. 17*:241-245, 1999, Hagstrom *et al., Blood 95*:2536-2542, 2000).

The ribosome binding site is located at or near the initiation codon. Examples of preferred ribosome binding sites include CCACCAUGG, CCGCCAUGG, and ACCAUGG, where AUG is the initiation codon. (Kozak, *Cell 44*:283-292, 1986). Another example of a ribosome binding site is GCCACCAUGG (SEQ. ID. NO. 12).

The polyadenylation signal is responsible for cleaving the transcribed RNA and the addition of a poly (A) tail to the RNA. The polyadenylation signal in higher eukaryotes contains an AAUAAA sequence about 11-30 nucleotides from the polyadenylation addition site. The AAUAAA sequence is involved in signaling RNA cleavage. (Lewin, Genes IV, Oxford University Press, NY, 1990.) The poly (A) tail is important for the mRNA processing.

Polyadenylation signals that can be used as part of a gene expression cassette include the minimal rabbit β -globin polyadenylation signal and the bovine growth hormone polyadenylation (BGH). (Xu *et al., Gene 272*:149-156, 2001, Post *et*

al., U.S. Patent U. S. 5,122,458.) Additional examples include the Synthetic Polyadenylation Signal (SPA) and SV40 polyadenylation signal. The SPA sequence is as follows: AAUAAAAGAUCUUUAUUUUCAUUAGAUCUGUGUG UUGGUUUUUUGUGUG (SEQ. ID. NO. 13).

Examples of additional regulatory elements useful for enhancing or regulating gene expression or polypeptide processing that may be present include an enhancer, a leader sequence and an operator. An enhancer region increases transcription. Examples of enhancer regions include the CMV enhancer and the SV40 enhancer. (Hitt *et al., Methods in Molecular Genetics 7*:13-30, 1995, Xu, *et al., Gene 272*:149-156, 2001.) An enhancer region can be associated with a promoter.

A leader sequence is an amino acid region on a polypeptide that directs the polypeptide into the proteasome. Nucleic acid encoding the leader sequence is 5' of a structural gene and is transcribed along the structural gene. An example of a leader sequences is tPA.

An operator sequence can be used to regulate gene expression. For example, the Tet operator sequence can be used to repress gene expression.

II. THERAPEUTIC VECTORS

Nucleic acid encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide can be introduced into a patient using vectors suitable for therapeutic administration. Suitable vectors can deliver nucleic acid into a target cell without causing an unacceptable side effect.

Cellular expression is achieved using a gene expression cassette encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide. The gene expression cassette contains regulatory elements for producing and processing a sufficient amount of nucleic acid inside a target cell to achieve a beneficial effect.

Examples of vectors that can be used for therapeutic applications include first and second generation adenovectors, helper dependent adenovectors, adeno-associated viral vectors, retroviral vectors, alpha virus vectors, Venezuelan Equine Encephalitis virus vector, and plasmid vectors. (Hitt, *et al., Advances in Pharmacology 40*:137-206, 1997, Johnston *et al.*, U.S. Patent No. 6,156,588, and Johnston *et al.*, International Publication Number WO 95/32733.) Preferred vectors for introducing a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide into a subject are first generation adenoviral vectors and plasmid DNA vectors.

A. First Generation Adenovectors

First generation adenovector for expressing a gene expression cassette contain the expression cassette in an E1 and optionally E3 deleted recombinant adenovirus genome. The deletion in the E1 region is sufficiently large to remove elements needed for adenoviral replication.

First generation adenovectors for expressing a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide contain a E1 and E3 deleted recombinant adenovirus genome. The deletion in the E1 region is sufficiently large to remove elements needed for adenoviral replication. The combinations of deletions of the E1 and E3 regions are sufficiently large to accommodate a gene expression cassette encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide.

The adenovirus has a double-stranded linear genome with inverted terminal repeats at both ends. During viral replication, the genome is packaged inside a viral capsid to form a virion. The virus enters its target cell through viral attachment followed by internalization. (Hitt *et al., Advances in Pharmacology 40*:137-206, 1997.)

Adenovectors can be based on different adenovirus serotypes such as those found in humans or animals. Examples of animal adenoviruses include bovine, porcine, chimp, murine, canine, and avian (CELO). Preferred adenovectors are based on human serotypes, more preferably Group B, C, or D serotypes. Examples of human adenovirus Group B, C, D, or E serotypes include types 2 ("Ad2"), 4 ("Ad4"), 5 ("Ad5"), 6 ("Ad6"), 24 ("Ad24"), 26 ("Ad26"), 34 ("Ad34") and 35 ("Ad35"). Adenovectors can contain regions from a single adenovirus or from two or more adenovirus.

In different embodiments adenovectors are based on Ad5, Ad6, or a combination thereof. Ad5 is described by Chroboczek, *et al., J. Virology 186*:280-285, 1992. Ad6 is described in Figures 7A-7N. An Ad6 based vector containing Ad5 regions is described in the Example section provided below.

Adenovectors do not need to have their E1 and E3 regions completely removed. Rather, a sufficient amount the E1 region is removed to render the vector replication incompetent in the absence of the E1 proteins being supplied in *trans*; and the E1 deletion or the combination of the E1 and E3 deletions are sufficiently large enough to accommodate a gene expression cassette.

E1 deletions can be obtained starting at about base pair 342 going up to about base pair 3523 of Ad5, or a corresponding region from other adenoviruses.

Preferably, the deleted region involves removing a region from about base pair 450 to about base pair 3511 of Ad5, or a corresponding region from other adenoviruses. Larger E1 region deletions starting at about base pair 341 removes elements that facilitate virus packaging.

E3 deletions can be obtained starting at about base pair 27865 to about base pair 30995 of Ad5, or the corresponding region of other adenovectors. Preferably the deletion region involves removing a region from about base pair 28134 up to about base pair 30817 of Ad5, or the corresponding region of other adenovectors.

The combination of deletions to the E1 region and optionally the E3 region should be sufficiently large so that the overall size of the recombinant genome containing the gene expression cassette does not exceed about 105% of the wild type adenovirus genome. For example, as recombinant adenovirus Ad5 genomes increase size above about 105% the genome becomes unstable. (Bett *et al., Journal of Virology 67*:5911-5921, 1993.)

Preferably, the size of the recombinant adenovirus genome containing the gene expression cassette is about 85% to about 105% the size of the wild type adenovirus genome. In different embodiments, the size of the recombinant adenovirus genome containing the expression cassette is about 100% to about 105.2%, or about 100%, the size of the wild type genome.

Approximately 7,500 kb can be inserted into an adenovirus genome with a E1 and E3 deletion. Without any deletion, the Ad5 genome is 35,935 base pairs and the Ad6 genome is 35,759 base pairs.

Replication of first generation adenovectors can be performed by supplying the E1 gene products in *trans*. The E1 gene product can be supplied in *trans*, for example, by using cell lines that have been transformed with the adenovirus E1 region. Examples of cells and cells lines transformed with the adenovirus E1 region are HEK 293 cells, 911 cells, PERC.6™ cells, and transfected primary human aminocytes cells. (Graham *et al., Journal of Virology 36*:59-72, 1977, Schiedner *et al., Human Gene Therapy 11*:2105-2116, 2000, Fallaux *et al., Human Gene Therapy* 9:1909-1917, 1998, Bout *et al.*, U.S. Patent No. 6,033,908.)

A Met-NS3-NS4A-NS4B-NS5A-NS5B expression cassette should be inserted into a recombinant adenovirus genome in the region corresponding to the deleted E1 region or the deleted E3 region. The expression cassette can have a parallel or anti-parallel orientation. In a parallel orientation the transcription direction

of the inserted gene is the same direction as the deleted E1 or E3 gene. In an anti-parallel orientation transcription the opposite strand serves as a template and the transcription direction is in the opposite direction.

In an embodiment of the present invention the adenovector has a gene expression cassette inserted in the E1 deleted region. The vector contains:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) a gene expression cassette in a E1 parallel or E1 anti-parallel orientation joined to the first region;

c) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to the expression cassette;

d) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to the second region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to the third region; and

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6 joined to the fourth region.

In another embodiment of the present invention the adenovector has an expression cassette inserted in the E3 deleted region. The vector contains:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to the first region;

c) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to the second region;

d) a gene expression cassette in a E3 parallel or E3 anti-parallel orientation joined to the third region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to the gene expression cassette; and

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to the fourth region.

In preferred different embodiments concerning adenovirus regions that are present: (1) the first, second, third, fourth, and fifth region corresponds to Ad5; (2) the first, second, third, fourth, and fifth region corresponds to Ad6; and (3) the first region corresponds to Ad5, the second region corresponds to Ad5, the third region corresponds to Ad6, the fourth region corresponds to Ad6, and the fifth region corresponds to Ad5.

B. DNA Plasmid Vectors

DNA vaccine plasmid vectors contain a gene expression cassette along with elements facilitating replication and preferably vector selection. Preferred elements provide for replication in non-mammalian cells and a selectable marker. The vectors should not contain elements providing for replication in human cells or for integration into human nucleic acid.

The selectable marker facilitates selection of nucleic acids containing the marker. Preferred selectable markers are those that confer antibiotic resistance. Examples of antibiotic selection genes include nucleic acid encoding resistance to ampicillin, neomycin, and kanamycin.

Suitable DNA vaccine vectors can be produced starting with a plasmid containing a bacterial origin of replication and a selectable marker. Examples of bacterial origins of replication providing for higher yields include the ColE1 plasmid-derived bacterial origin of replication. (Donnelly *et al., Annu. Rev. Immunol. 15*:617-648, 1997.)

The presence of the bacterial origin of replication and selectable marker allows for the production of the DNA vector in a bacterial strain such as *E. coli*. The selectable marker is used to eliminate bacteria not containing the DNA vector.

III. AD6 RECOMBINANT NUCLEIC ACID

Ad6 recombinant nucleic acid comprises an Ad6 region substantially similar to an Ad6 region found in SEQ. ID. NO. 8, and a region not present in Ad6 nucleic acid. Recombinant nucleic acid comprising Ad6 regions have different uses such as in producing different Ad6 regions, as intermediates in the production of Ad6 based vectors, and as a vector for delivering a recombinant gene.

As depicted in Figure 9, the genomic organization of Ad6 is very similar to the genomic organization of Ad5. The homology between Ad5 and Ad6 is approximately 98%.

In different embodiments, the Ad6 recombinant nucleic acid comprises a nucleotide region substantially similar to E1A, E1B, E2B, E2A, E3, E4, L1, L2, L3, or L4, or any combination thereof. A substantially similar nucleic acid region to an Ad6 region has a nucleotide sequence identity of at least 65%, at least 75%, at least 85%, at least 95%, at least 99% or 100%; or a nucleotide difference of 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 1-11, 1-12, 1-13, 1-14, 1-15, 1-16, 1-17, 1-18, 1-19, 1-20, 1-25, 1-30, 1-35, 1-40, 1-45, or 1-50 nucleotides. Techniques and embodiments for determining substantially similar nucleic acid sequences are described in Section I.B. *supra.*

Preferably, the recombinant Ad6 nucleic acid contains an expression cassette coding for a polypeptide not found in Ad6. Examples of expression cassettes include those coding for HCV regions and those coding for other types of polypeptides.

Different types of adenoviral vectors can be produced incorporating different amounts of Ad6, such as first and second generation adenovectors. As noted in Section II.A. *supra.* first generation adenovectors are defective in E1 and can replicate when E1 is supplied *in trans.*

Second generation adenovectors contain less adenoviral genome than first generation vectors and can be used in conjugation with complementing cell lines and/or helper vectors supplying adenoviral proteins. Second generation adenovectors are described in different references such as Russell, *Journal of General Virology 81*:2573-2604, 2000; Hitt *et al.*, 1997, Human Ad vectors for Gene Transfer, Advances in Pharmacology, Vol 40 Academic Press.

In an embodiment of the present invention, the Ad6 recombinant nucleic acid is an adenovirus vector defective in E1 that is able to replicate when E1 is

supplied *in trans*. Expression cassettes can be inserted into a deleted E1 region and/or a deleted E3 region.

An example of an Ad6 based adenoviral vector with an expression cassette provided in a deleted E1 region comprises or consists of:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) a gene expression cassette in a E1 parallel or E1 anti-parallel orientation joined to the first region;

c) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to the expression cassette;

d) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to the second region;

e) an optionally present fourth region from about base pair 28134 to about base pair 30817 corresponding to Ad5, or from about base pair 28157 to about base pair 30788 corresponding to Ad6, joined to the third region;

f) a fifth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, wherein the fifth region is joined to the fourth region if the fourth region is present, or the fifth is joined to the third region if the fourth region is not present; and

g) a sixth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to the fifth region;

wherein at least one Ad6 region is present.

In different embodiments of the invention, all of the regions are from Ad6; all of the regions expect for the first and second are from Ad6; and 1, 2, 3, or 4 regions selected from the second, third, fourth, and fifth regions are from Ad6.

An example of an Ad6 based adenoviral vector with an expression cassette provided in a deleted E3 region comprises or consists of:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to the first region;

c) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to the second region;

d) a gene expression cassette in a E3 parallel or E3 anti-parallel orientation joined to the third region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to the gene expression cassette; and

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to the fourth region;

wherein at least one Ad6 region is present.

In different embodiment of the invention, all of the regions are from Ad6; all of the regions expect for the first and second are from Ad6; and 1, 2, 3, or 4 regions selected from the second, third, fourth and fifth regions are from Ad6.

IV. VECTOR PRODUCTION

Vectors can be produced using recombinant nucleic acid techniques such as those involving the use of restriction enzymes, nucleic acid ligation, and homologous recombination. Recombinant nucleic acid techniques are well known in the art. (Ausubel, *Current Protocols in Molecular Biology,* John Wiley, 1987-1998, and Sambrook *et al.*, *Molecular Cloning, A Laboratory Manual,* 2nd Edition, Cold Spring Harbor Laboratory Press, 1989.)

Intermediate vectors are used to derive a therapeutic vector or to transfer an expression cassette or portion thereof from one vector to another vector. Examples of intermediate vectors include adenovirus genome plasmids and shuttle vectors.

Useful elements in an intermediate vector include an origin of replication, a selectable marker, homologous recombination regions, and convenient restriction sites. Convenient restriction sites can be used to facilitate cloning or release of a nucleic acid sequence.

Homologous recombination regions provide nucleic acid sequence regions that are homologous to a target region in another nucleic acid molecule. The homologous regions flank the nucleic acid sequence that is being inserted into the target region. In different embodiments homologous regions are preferably about 150 to 600 nucleotides in length, or about 100 to 500 nucleotides in length.

An embodiment of the present invention describes a shuttle vector containing a Met-NS3-NS4A-NS4B-NS5A-NS5B expression cassette, a selectable marker, a bacterial origin of replication, a first adenovirus homology region and a second adenovirus homologous region that target the expression cassette to insert in or replace an E1 region. The first and second homology regions flank the expression cassette. The first homology region contains at least about 100 base pairs substantially homologous to at least the right end (3' end) of a wild-type adenovirus region from about base pairs 4-450. The second homology contains at least about 100 base pairs substantially homologous to at least the left end (5' end) of Ad5 from about base pairs 3511-5792, or the corresponding region from another adenovirus.

Reference to "substantially homologous" indicates a sufficient degree of homology to specifically recombine with a target region. In different embodiments substantially homologous refers to at least 85%, at least 95%, or 100% sequence identity. Sequence identity can be calculated as described in Section I.B. *supra.*

One method of producing adenovectors is through the creation of an adenovirus genome plasmid containing an expression cassette. The pre-Adenovirus plasmid contains all the adenovirus sequences needed for replication in the desired complimenting cell line. The pre-Adenovirus plasmid is then digested with a restriction enzyme to release the viral ITR's and transfected into the complementing cell line for virus rescue. The ITR's must be released from plasmid sequences to allow replication to occur. Adenovector rescue results in the production on an adenovector containing the expression cassette.

A. Adenovirus Genome Plasmids

Adenovirus genome plasmids contain an adenovector sequence inside a longer-length plasmid (which may be a cosmid). The longer-length plasmid may contain additional elements such as those facilitating growth and selection in eukaryotic or bacterial cells depending upon the procedures employed to produce and maintain the plasmid. Techniques for producing adenovirus genome plasmids include those involving the use of shuttle vectors and homologous recombination, and those

involving the insertion of a gene expression cassette into an adenovirus cosmid. (Hitt *et al., Methods in Molecular Genetics* 7:13-30, 1995, Danthinne *et al., Gene Therapy* 7:1707-1714, 2000.)

Adenovirus genome plasmids preferably have a gene expression cassette inserted into a E1 or E3 deleted region. In an embodiment of the present invention, the adenovirus genome plasmid contains a gene expression cassette inserted in the E1 deleted region, an origin of replication, a selectable marker, and the recombinant adenovirus region is made up of:

a) a first adenovirus region from about base pair 1 to about base 450 corresponding to either Ad5 or Ad6;

b) a gene expression cassette in a E1 parallel or E1 anti-parallel orientation joined to the first region;

c) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to the expression cassette;

d) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to the second region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to the third region;

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to the fourth region, and

g) an optionally present E3 region corresponding to all or part of the E3 region present in Ad5 or Ad6, which may be present for smaller inserts taking into account the overall size of the desired adenovector.

In another embodiment of the present invention the recombinant adenovirus genome plasmid has the gene expression cassette inserted in the E3 deleted region. The vector contains an origin of replication, a selectable marker, and the following:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to the expression cassette;

c) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to the second region;

d) the gene expression cassette in a E3 parallel or E3 anti-parallel orientation joined to the third region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to the gene expression cassette; and

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to the fourth region.

In different embodiments concerning adenovirus regions that are present: (1) the first, second, third, fourth, and fifth region corresponds to Ad5; (2) the first, second, third, fourth, and fifth region corresponds to Ad6; and (3) the first region corresponds to Ad5, the second region corresponds to Ad5, the third region corresponds to Ad6, the fourth region corresponds to Ad6, and the fifth region corresponds to Ad5.

An embodiment of the present invention describes a method of making an adenovector involving a homologous recombination step to produce a adenovirus genome plasmid and an adenovirus rescue step. The homologous recombination step involves the use of a shuttle vector containing a Met-NS3-NS4A-NS4B-NS5A-NS5B expression cassette flanked by adenovirus homology regions. The adenovirus homology regions target the expression cassette into either the E1 or E3 deleted region.

In an embodiment of the present invention concerning the production of an adenovirus genome plasmid, the gene expression cassette is inserted into a vector comprising: a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6; a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to the second region; a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6,

joined to the second region; a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to the third region; and a fifth adenovirus region from about 33967 to about 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to the fourth region. The adenovirus genome plasmid should contain an origin of replication and a selectable marker, and may contain all or part of the Ad5 or Ad6 E3 region.

In different embodiments concerning adenovirus regions that are present: (1) the first, second, third, fourth, and fifth region corresponds to Ad5; (2) the first, second, third, fourth, and fifth region corresponds to Ad6; and (3) the first region corresponds to Ad5, the second region corresponds to Ad5, the third region corresponds to Ad6, the fourth region corresponds to Ad6, and the fifth region corresponds to Ad5.

B. Adenovector Rescue

An adenovector can be rescued from a recombinant adenovirus genome plasmid using techniques known in the art or described herein. Examples of techniques for adenovirus rescue well known in the art are provided by Hitt *et al.*, *Methods in Molecular Genetics* 7:13-30, 1995, and Danthinne *et al.*, *Gene Therapy* 7:1707-1714, 2000.

A preferred method of rescuing an adenovector described herein involves boosting adenoviral replication. Boosting adenoviral replication can be performed, for example, by supplying adenoviral functions such as E2 proteins (polymerase, pre-terminal protein and DNA binding protein) as well as E4 orf6 on a separate plasmid. Example 10 *infra.* illustrates the boosting of adenoviral replication to rescue an adenovector containing a codon optimized Met-NS3-NS4A-NS4B-NS5A-NS5B expression cassette.

V. PARTIAL-OPITIMIZED HCV ENCODING SEQUENCES

Partial optimization of HCV polyprotein encoding nucleic acid provides for a lesser amount of codons optimized for expression in a human than complete optimization. The overall objective is to provide the benefits of increased expression due to codon optimization, while facilitating the production of an adenovector containing HCV polyprotein encoding nucleic acid having optimized codons.

Complete optimization of an HCV polyprotein encoding sequence provides the most frequently observed human codon for each amino acid. Complete optimization can be performed using codon frequency tables well known in the art and using programs such as the BACKTRANSLATE program (Wisconsin Package version 10, Genetics Computer Group, GCG, Madison, Wisc.).

Partial optimization can be preformed on an entire HCV polyprotein encoding sequence that is present (*e.g.*, NS3-NS5B), or one or more local regions that are present. In different embodiments the GC content for the entire HCV encoded polyprotein that is present is no greater than at least about 65%; and the GC content for one or more local regions is no greater than about 70%.

Local regions are regions present in HCV encoding nucleic acid, and can vary in size. For example, local regions can be about 60, about 70, about 80, about 90 or about 100 nucleotides in length.

Partial optimization can be achieved by initially constructing an HCV encoding polyprotein sequence to be partially optimized based on a naturally ocurring sequence. Alternatively, an optimized HCV encoding sequence can be used as basis of comparison to produce a partial optimized sequence.

VI. HCV COMBINATION TREATMENT

The HCV Met-NS3-NS4A-NS4B-NS5A-NS5B vaccine can be used by itself to treat a patient, can be used in conjunction with other HCV therapeutics, and can be used with agents targeting other types of diseases. Additional therapeutics include additional therapeutic agents to treat HCV and diseases having a high prevalence in HCV infected persons. Agents targeting other types of disease include vaccines directed against HIV and HBV.

Additional therapeutics for treating HCV include vaccines and non-vaccine agents. (Zein, *Expert Opin. Investig. Drugs 10*:1457-1469, 2001.) Examples of additional HCV vaccines include vaccines designed to elicit an immune response against an HCV core antigen and the HCV E1, E2 or p7 region. Vaccine components can be naturally occurring HCV polypeptides, HCV mimotope polypeptides or nucleic acid encoding such polypeptides.

HCV mimotope polypeptides contain HCV epitopes, but have a different sequence than a naturally occurring HCV antigen. A HCV mimotope can be fused to a naturally occurring HCV antigen. References describing techniques for producing mimotopes in general and describing different HCV mimotopes are

provided in Felici *et al.* U.S. Patent No. 5,994,083 and Nicosia *et al.*, International Application Number WO 99/60132.

VII. PHARMACEUTICAL ADMINISTRATION

HCV vaccines can be formulated and administered to a patient using the guidance provided herein along with techniques well known in the art. Guidelines for pharmaceutical administration in general are provided in, for example, *Modern Vaccinology*, Ed. Kurstak, Plenum Med. Co. 1994; *Remington's Pharmaceutical Sciences 18th Edition*, Ed. Gennaro, Mack Publishing, 1990; and *Modern Pharmaceutics 2nd Edition*, Eds. Banker and Rhodes, Marcel Dekker, Inc., 1990, each of which are hereby incorporated by reference herein.

HCV vaccines can be administered by different routes such intravenous, intraperitoneal, subcutaneous, intramuscular, intradermal, impression through the skin, or nasal. A preferred route is intramuscular.

Intramuscular administration can be preformed using different techniques such as by injection with or without one or more electric pulses. Electric mediated transfer can assist genetic immunization by stimulating both humoral and cellular immune responses.

Vaccine injection can be performed using different techniques, such as by employing a needle or a needless injection system. An example of a needless injection system is a jet injection device. (Donnelly *et al.*, International Publication Number WO 99/52463.)

A. Electrically Mediated Transfer

Electrically mediated transfer or Gene Electro-Transfer (GET) can be performed by delivering suitable electric pulses after nucleic acid injection. (See Mathiesen, International Publication Number WO 98/43702). Plasmid injection and electroporation can be performed using stainless needles. Needles can be used in couples, triplets or more complex patterns. In one configuration the needles are soldered on a printed circuit board that is a mechanical support and connects the needles to the electrical field generator by means of suitable cables.

The electrical stimulus is given in the form of electrical pulses. Pulses can be of different forms (square, sinusoidal, triangular, exponential decay) and different polarity (monopolar of positive or negative polarity, bipolar). Pulses can be delivered either at constant voltage or constant current modality.

Different patterns of electric treatment can be used to introduce nucleic acid vaccines including HCV and other nucleic acid vaccines into a patient. Possible patterns of electric treatment include the following:

Treatment 1: 10 trains of 1000 square bipolar pulses delivered every other second, pulse length 0.2 msec/phase, frequency 1000 Hz, constant voltage mode, 45 Volts/phase, floating current.

Treatment 2: 2 trains of 100 square bipolar pulses delivered every other second, pulse length 2 msec/phase, frequency 100 Hz, constant current mode, 100 mA/phase, floating voltage.

Treatment 3: 2 trains of bipolar pulses at a pulse length of about 2 msec/phase, for a total length of about 3 seconds, where the actual current going through the tissue is fixed at about 50 mA.

Electric pulses are delivered through an electric field generator. A suitable generator can be composed of three independent hardware elements assembled in a common chassis and driven by a portable PC which runs the driving program. The software manages both basic and accessory functions. The elements of the device are: (1) signal generator driven by a microprocessor, (2) power amplifier and (3) digital oscilloscope.

The signal generator delivers signals having arbitrary frequency and shape in a given range under software control. The same software has an interactive editor for the waveform to be delivered. The generator features a digitally controlled current limiting device (a safety feature to control the maximal current output). The power amplifier can amplify the signal generated up to +/- 150 V. The oscilloscope is digital and is able to sample both the voltage and the current being delivered by the amplifier.

B. Pharmaceutical Carriers

Pharmaceutically acceptable carriers facilitate storage and administration of a vaccine to a subject. Examples of pharmaceutically acceptable carriers are described herein. Additional pharmaceutical acceptable carriers are well known in the art.

Pharmaceutically acceptable carriers may contain different components such a buffer, normal saline or phosphate buffered saline, sucrose, salts and polysorbate. An example of a pharmaceutically acceptable carrier is follows: 2.5-10 mM TRIS buffer, preferably about 5 mM TRIS buffer; 25-100 mM NaCl, preferably

about 75 mM NaCl; 2.5-10% sucrose, preferably about 5% sucrose; 0.01 -2 mM $MgCl_2$; and 0.001%-0.01% polysorbate 80 (plant derived). The pH is preferably from about 7.0-9.0, more preferably about 8.0. A specific example of a carrier contains 5 mM TRIS, 75 mM NaCl, 5% sucrose, 1 mM $MgCl_2$, 0.005% polysorbate 80 at pH 8.0.

C. Dosing Regimes

Suitable dosing regimens can be determined taking into account the efficacy of a particular vaccine and factors such as age, weight, sex and medical condition of a patient; the route of administration; the desired effect; and the number of doses. The efficacy of a particular vaccine depends on different factors such as the ability of a particular vaccine to produce polypeptide that is expressed and processed in a cell and presented in the context of MHC class I and II complexes.

HCV encoding nucleic acid administered to a patient can be part of different types of vectors including viral vectors such as adenovector, and DNA plasmid vaccines. In different embodiments concerning administration of a DNA plasmid, about 0.1 to 10 mg of plasmid is administered to a patient, and about 1 to 5 mg of plasmid is administered to a patient. In different embodiments concerning administration of a viral vector, preferably an adenoviral vector, about 10^5 to 10^{11} viral particles are administered to a patient, and about 10^7 to 10^{10} viral particles are administered to a patient.

Viral vector vaccines and DNA plasmid vaccines may be administered alone, or may be part of a prime and boost administration regimen. A mixed modality priming and booster inoculation involves either priming with a DNA vaccine and boosting with viral vector vaccine, or priming with a viral vector vaccine and boosting with a DNA vaccine.

Multiple priming, for example, about to 2-4 or more may be used. The length of time between priming and boost may typically vary from about four months to a year, but other time frames may be used. The use of a priming regimen with a DNA vaccine may be preferred in situations where a person has a pre-existing anti-adenovirus immune response.

In an embodiment of the present invention, $1x10^7$ to $1x10^{12}$ particles and preferably about $1x10^{10}$ to $1x10^{11}$ particles of adenovector is administered directly into muscle tissue. Following initial vaccination a boost is performed with an adenovector or DNA vaccine.

In another embodiment of the present invention initial vaccination is performed with a DNA vaccine directly into muscle tissue. Following initial vaccination a boost is performed with an adenovector or DNA vaccine.

Agents such as interleukin-12, GM-CSF, B7-1, B7-2, IP10, Mig-1 can be coadministered to boost the immune response. The agents can be coadministered as proteins or through use of nucleic acid vectors.

D. Heterologous Prime-Boost

Heterologous prime-boost is a mixed modality involving the use of one type of viral vector for priming and another type of viral vector for boosting. The heterologous prime-boost can involve related vectors such as vectors based on different adenovirus serotypes and more distantly related viruses such adenovirus and poxvirus. The use of poxvirus and adenovirus vectors to protect mice against malaria is illustrated by Gilbert *et al.*, *Vaccine* 20:1039-1045, 2002.

Different embodiments concerning priming and boosting involve the following types of vectors expressing desired antigens such as Met-NS3-NS4A-NS4B-NS5A-NS5B: Ad5 vector followed by Ad6 vector; Ad6 vector followed by Ad5 vector; Ad5 vector followed by poxvirus vector; poxvirus vector followed by Ad5 vector; Ad6 vector followed by poxvirus vector; and poxvirus vector followed by Ad6 vector.

The length of time between priming and boosting typically varies from about four months to a year, but other time frames may be used. The minimum time frame should be sufficient to allow for an immunological rest. In an embodiment, this rest is for a period of at least 6 months. Priming may involve multiple priming with one type of vector, such as 2-4 primings.

Expression cassettes present in a poxvirus vector should contain a promoter either native to, or derived from, the poxvirus of interest or another poxvirus member. Different strategies for constructing and employing different types of poxvirus based vectors including those based on vaccinia virus, modified vaccinia virus, avipoxvirus, raccoon poxvirus, modified vaccinia virus Ankara, canarypoxviruses (such as ALVAC), fowlpoxviruses, cowpoxviruses, and NYVAC are well known in the art. (Moss, *Current Topics in Microbiology and Immunology 158*:25-38, 1982; Earl *et al.*, In *Current Protocols in Molecular Biology*, Ausubel *et al.* eds., New York: Greene Publishing Associates & Wiley Interscience; 1991:16.16.1-16.16.7, Child *et al.*, *Virology* 174(2):625-9, 1990; Tartaglia *et al.*,

Virology 188:217-232, 1992; U.S. Patent Nos., 4,603,112, 4,722,848, 4,769,330, 5,110,587, 5,174,993, 5,185,146, 5,266,313, 5,505,941, 5,863,542, and 5,942,235.

E. Adjuvants

HCV vaccines can be formulated with an adjuvant. Adjuvants are particularly useful for DNA plasmid vaccines. Examples of adjuvants are alum, $AlPO_4$, alhydrogel, Lipid-A and derivatives or variants thereof, Freund's incomplete adjuvant, neutral liposomes, liposomes containing the vaccine and cytokines, non-ionic block copolymers, and chemokines.

Non-ionic block polymers containing polyoxyethylene (POE) and polyxylpropylene (POP), such as POE-POP-POE block copolymers may be used as an adjuvant. (Newman *et al., Critical Reviews in Therapeutic Drug Carrier Systems 15*:89-142, 1998.) The immune response of a nucleic acid can be enhanced using a non-ionic block copolymer combined with an anionic surfactant.

A specific example of an adjuvant formulation is one containing CRL-1005 (CytRx Research Laboratories), DNA, and benzylalkonium chloride (BAK). The formulation can be prepared by adding pure polymer to a cold (< 5°C) solution of plasmid DNA in PBS using a positive displacement pipette. The solution is then vortexed to solubilize the polymer. After complete solubilization of the polymer a clear solution is obtained at temperatures below the cloud point of the polymer (~6-7°C). Approximately 4 mM BAK is then added to the DNA/CRL-1005 solution in PBS, by slow addition of a dilute solution of BAK dissolved in PBS. The initial DNA concentration is approximately 6 mg/mL before the addition of polymer and BAK, and the final DNA concentration is about 5 mg/mL. After BAK addition the formulation is vortexed extensively, while the temperature is allowed to increase from ~ 2°C to above the cloud point. The formulation is then placed on ice to decrease the temperature below the cloud point. Then, the formulation is vortexed while the temperature is allowed to increase from ~2°C to above the cloud point. Cooling and mixing while the temperature is allowed to increase from ~2°C to above the cloud point is repeated several times, until the particle size of the formulation is about 200-500 nm, as measured by dynamic light scattering. The formulation is then stored on ice until the solution is clear, then placed in storage at –70°C. Before use, the formulation is allowed to thaw at room temperature.

F. Vaccine Storage

Adenovector and DNA vaccines can be stored using different types of buffers. For example, buffer A105 described in Example 9 *infra.* can be used to for vector storage.

Storage of DNA can be enhanced by removal or chelation of trace metal ions. Reagents such as succinic or malic acid, and chelators can be used to enhance DNA vaccine stability. Examples of chelators include multiple phosphate ligands and EDTA. The inclusion of non-reducing free radical scavengers, such as ethanol or glycerol, can also be useful to prevent damage of DNA plasmid from free radical production. Furthermore, the buffer type, pH, salt concentration, light exposure, as well as the type of sterilization process used to prepare the vials, may be controlled in the formulation to optimize the stability of the DNA vaccine.

VII. EXAMPLES

Examples are provided below to further illustrate different features of the present invention. The examples also illustrate useful methodology for practicing the invention. These examples do not limit the claimed invention.

Example 1: Met-NS3-NS4A-NS4B-NS5A-NS5B Expression Cassettes

Different gene expression cassettes encoding HCV NS3-NS4A-NS4B-NS5A-NS5B were constructed based on a 1b subtype HCV BK strain. The encoded sequences had either (1) an active NS5B sequence ("NS"), (2) an inactive NS5B sequence ("NSmut"), (3) a codon optimized sequence with an inactive NS5B sequence ("NSOPTmut"). The expression cassettes also contained a CMV promoter/enhancer and the BGH polyadenylation signal.

The NS nucleotide sequence (SEQ. ID. NO. 5) differs from HCV BK strain GenBank accession number M58335 by 30 out of 5952 nucleotides. The NS amino acid sequence (SEQ. ID. NO. 6) differs from the corresponding 1b genotype HCV BK strain by 7 out of 1984 amino acids. To allow for initiation of translation an ATG codon is present at the 5' end of the NS sequence. A TGA termination sequence is present at the 3' end of the NS sequence.

The NSmut nucleotide sequence (SEQ. ID. NO. 2, Figure 2), is similar to the NS sequence. The differences between NSmut and NS include NSmut having an altered NS5B catalytic site; an optimal ribosome binding site at the 5' end; and a TAAA termination sequence at the 3' end. The alterations in NS5B comprise bases

5138 to 5146, which encode amino acids 1711 to 1713. The alterations result in a change of amino acids GlyAspAsp into AlaAlaGly and creates an inactive form of the NS5B RNA-dependent RNA-polymerase NS5B.

The NSOPTmut sequence (SEQ. ID. NO. 3, Figure 3) was designed based on the amino acid sequence encoded by NSmut. The NSmut amino acid sequence was back translated into a nucleotide sequence with the GCG (Wisconsin Package version 10, Genetics Computer Group, GCG, Madison, Wisc.) BACKTRANSLATE program. To generate a NSOPTmut nucleotide sequence where each amino acid is coded for by the corresponding most frequently observed human codon, the program was run choosing as parameter the generation of the most probable nucleotide sequence and specifying the codon frequency table of highly expressed human genes (human_high.cod) available within the GCG Package as translation scheme.

<u>Example 2: Generation pV1Jns plasmid with NS, NSmut or NSOPTmut Sequences</u>

pV1Jns plasmids containing either the NS sequence, NSmut sequence or NSOPTmut sequences were generated and characterised as follows:

pV1Jns Plasmid with the NS Sequence

The coding region Met-NS3-NS4A-NS4B-NS5A and the coding region Met-NS3-NS4A-NS4B-NS5A-NS5B from a HCV BK type strain (Tomei *et al., J. Virol. 67*:4017-4026, 1993) were cloned into pcDNA3 plasmid (Invitrogen), generating pcD3-5a and pcD3-5b vectors, respectively. PcD3-5A was digested with Hind III, blunt-ended with Klenow fill-in and subsequently digested with Xba I, to generate a fragment corresponding to the coding region of Met-NS3-NS4A-NS4B-NS5A. The fragment was cloned into pV1Jns-poly, digested with Bgl II blunt-ended with Klenow fill-in and subsequently digested with Xba I, generating pV1JnsNS3-5A.

pV1Jns-poly is a derivative of pV1JnsA plasmid (Montgomery et al., *DNA and Cell Biol. 12*:777-783, 1993), modified by insertion of a polylinker containing recognition sites for XbaI, PmeI, PacI into the unique BglII and NotI restriction sites. The pV1Jns plasmid with the NS sequence (pV1JnsNS3-5B) was obtained by homologous recombination into the bacterial strain BJ5183, co-transforming pV1JNS3-5A linearized with XbaI and NotI digestion and a PCR fragment containing approximately 200 bp of NS5A, NS5B coding sequence and

approximately 60 bp of the BGH polyadenylation signal. The resulting plasmid represents pV1Jns-NS.

pV1Jns-NS can be summarized as follows:

Bases	1 to 1881 of pV1JnsA
an additional	AGCTT
then the	Met-NS3-NS5B sequence (SEQ. ID. NO. 5)
then the	wt TGA stop
an additional	TCTAGAGCGTTTAAACCCTTAATTAAGG (SEQ. ID. NO. 14)
Bases	1912 to 4909 of pV1JnsA

pV1Jns Plasmid with the NSmut Sequence

The V1JnsNS3-5A plasmid was modified at the 5' of the NS3 coding sequence by addition of a full Kozak sequence. The plasmid (V1JNS3-5Akozak) was obtained by homologous recombination into the bacterial strain BJ5183, co-transforming V1JNS3-5A linearized by *AflII* digestion and a PCR fragment containing the proximal part of Intron A, the restriction site BglII, a full Kozak translation initiation sequence and part of the NS3 coding sequence.

The resulting plasmid (V1JNS3-5Akozak) was linearized with Xba I digestion and co-transformed into the bacterial strain BJ5183 with a PCR fragment, containing approximately 200 bp of NS5A, the NS5B mutated sequence, the strong translation termination TAAA and approximately 60 bp of the BGH polyadenylation signal. The PCR fragment was obtained by assembling two 22bp-overlapping fragments where mutations were introduced by the oligonucleotides used for their amplification. The resulting plasmid represents pV1Jns-NSmut.

pV1Jns-NSmut can be summarized as follows:

Bases	1 to 1882 of pV1JnsA
then the	kozak Met-NS3-NS5B(mut) TAAA sequence (SEQ. ID. NO. 2)
an additional	TCTAGA
Bases	1925 to 4909 of pV1JnsA

pV1Jns Plasmid with the NSOPTmut Sequence

The human codon-optimized synthetic gene (NSOPTmut) with mutated NS5B to abrogate enzymatic activity, full Kozak translation initiation sequence and a strong translation termination was digested with BamHI and SalI

restriction sites present at the 5' and 3' end of the gene. The gene was then cloned into the BglII and SalI restriction sites present in the polylinker of pV1JnsA plasmid, generating pV1Jns-NSOPTmut.

pV1Jns-NSOPTmut can be summarized as follows:

Bases	1 to 1881 of pV1JnsA
an additional	C
then	kozak Met-NS3-NS5B(optmut) TAAA sequence (SEQ. ID. NO. 3)
an additional	TTTAAATGTTTAAAC (SEQ. ID. NO. 15)
Bases	1905 to 4909 of pV1JnsA

Plasmids Characterization

Expression of HCV NS proteins was tested by transfection of HEK 293 cells, grown in 10% FCS/DMEM supplemented by L-glutamine (final 4 mM). Twenty-four hours before transfection, cells were plated in 6-well 35 mm diameter, to reach 90-95% confluence on the day of transfection. Forty nanograms of plasmid DNA (previously assessed as a non-saturating DNA amount) were co-transfected with 100 ng of pRSV-Luc plasmid containing the luciferase reporter gene under the control of Rous sarcoma virus promoter, using the LIPOFECTAMINE 2000 reagent. Cells were kept in a CO_2 incubator for 48 hours at 37 °C.

Cell extracts were prepared in 1% Triton/TEN buffer. The extracts were normalized for Luciferase activity, and run in serial dilution on 10% SDS-acrylamide gel. Proteins were transferred on nitrocellulose and assayed with antibodies directed against NS3, NS5A and NS5B to assess strength of expression and correct proteolytic cleavage. Mock-transfected cells were used as a negative control. Results from representative experiments testing pV1JnsNS, pV1JnsNSmut and pV1JnsNSOPTmut are shown in Figure 12.

Example 3: Mice Immunization with Plasmid DNA Vectors

The DNA plasmids pV1Jns-NS, pV1Jns-NSmut and pV1Jns-NSOPTmut were injected in different mice strains to evaluate their potential to elicit anti-HCV immune responses. Two different strains (Balb/C and C57Black6, N=9-10) were injected intramuscularly with 25 or 50 μg of DNA followed by electrical pluses. Each animal received two doses at three weeks interval.

Humoral immune response elicited in C57Black6 mice against the NS3 protein was measured in post dose two sera by ELISA on bacterially expressed NS3

protease domain. Antibodies specific for the tested antigen were detected in animals immunized with all three vectors with geometric mean titers (GMT) ranging from 94000 to 133000 (Tables 1-3).

Table 1: pV1jns-NS

										GMT
Mice n.	1	2	3	4	5	6	7	8	9	
Titer	105466	891980	78799	39496	543542	182139	32351	95028	67800	94553

Table 2: pV1jns-NSmut

											GMT
Mice n.	11	12	13	14	15	16	17	18	19	20	
Titer	202981	55670	130786	49748	17672	174958	44304	37337	78182	193695	75083

Table 3: pV1jns-NSOPTmut

											GMT
Mice n.	21	22	23	24	25	26	27	28	29	30	
Titer	310349	43645	63496	82174	630778	297259	66861	146735	173506	77732	133165

A T cell response was measured in C57Black6 mice immunized with two intramuscular injections at three weeks interval with 25 μg of plasmid DNA. Quantitative ELIspot assay was performed to determine the number of IFNγ secreting T cells in response to five pools of 20mer peptides overlapping by ten residues encompassing the NS3-NS5B sequence. Specific CD8+ response was analyzed by the same assay using a 20mer peptide encompassing a CD8+ epitope for C57Black6 mice (pep1480).

Cells secreting IFNγ in an antigen specific-manner were detected using a standard ELIspot assay. T cell response in C57Black6 mice immunized with two intramuscular injections at three weeks interval with 50 μg of plasmid DNA, was

analyzed by the same ELIspot assay measuring the number of IFNγ secreting T cells in response to five pools of 20mer peptides overlapping by ten residues encompassing the NS3-NS5B sequence.

Spleen cells were prepared from immunized mice and re-suspended in R10 medium (RPMI 1640 supplemented with 10% FCS, 2 mM L-Glutamine, 50 U/ml-50μg/ml Penicillin/Streptomycin, 10 mM Hepes, 50 μM 2-mercapto-ethanol). Multiscreen 96-well Filtration Plates (Millipore, Cat. No. MAIPS4510, Millipore Corporation, 80 Ashby Road Bedford, MA) were coated with purified rat anti-mouse INFγ antibody (PharMingen, Cat. No. 18181D, PharmiMingen, 10975 Torreyana Road, San Diego, California 92121-1111 USA). After overnight incubation, plates were washed with PBS 1X/0.005% Tween and blocked with 250 μl/well of R10 medium.

Splenocytes from immunized mice were prepared and incubated for twenty-four hours in the presence or absence of 10 μM peptide at a density of 2.5 X 10^5/well or 5 X 10^5/well. After extensive washing (PBS 1X/0.005% Tween), biotinylated rat anti-mouse IFNγ antibody (PharMingen, Cat. No. 18112D, PharMingen, 10975 Torreyana Road, San Diego, California 92121-1111 USA) was added and incubated overnight at 4° C. For development, streptavidin-AKP (PharMingen, Cat. No. 13043E, PharMingen, 10975 Torreyana Road, San Diego, California 92121-1111 USA) and 1-Step™ NBT-BCIP development solution (Pierce, Cat. No. 34042, Pierce, P.O. Box 117, Rockford, IL 61105 USA) were added.

Pools of 20mer overlapping peptides encompassing the entire sequence of the HCV BK strain NS3 to NS5B were used to reveal HCV-specific IFNγ-secreting T cells. Similarly a single 20mer peptide encompassing a CD8+ epitope for C57Black6 mice was used to detect CD8 response. Representative data from groups of C57Black6 and Balb/C mice (N=9-10) immunized with two injections of 25 or 50 μg of plasmid vectors pV1Jns-NS, pV1Jns-NSmut and pV1Jns-NSOPTmut are shown in Figures 13A and 13B.

<u>Example 4: Immunization of Rhesus Macaques</u>

Rhesus macaques (N=3) were immunized by intramuscular injection with 5mg of plasmid pV1Jns-NSOPTmut in 7.5mg/ml CRL1005, Benzalkonium chloride 0.6 mM. Each animal received two doses in the deltoid muscle at 0, and 4 weeks.

CMI was measured at different time points by IFN-γ ELISPOT. This assay measures HCV antigen-specific CD8+ and CD4+ T lymphocyte responses, and can be used for a variety of mammals, such as humans, rhesus monkeys, mice, and rats.

The use of a specific peptide or a pool of peptides can simplify antigen presentation in CTL cytotoxicity assays, interferon-gamma ELISPOT assays and interferon-gamma intracellular staining assays. Peptides based on the amino acid sequence of various HCV proteins (core, E2, NS3, NS4A, NS4B, NS5A, NS5B) were prepared for use in these assays to measure immune responses in HCV DNA and adenovirus vector vaccinated rhesus monkeys, as well as in HCV-infected humans. The individual peptides are overlapping 20-mers, offset by 10 amino acids. Large pools of peptides can be used to detect an overall response to HCV proteins while smaller pools and individual peptides may be used to define the epitope specificity of a response.

IFNγ ELISPOT

The IFNγ-ELISPOT assay provides a quantitative determination of HCV-specific T lymphocyte responses. PBMC are serially diluted and placed in microplate wells coated with anti-rhesus IFN-γ antibody (MD-1 U-Cytech). They are cultured with a HCV peptide pool for 20 hours, resulting in the restimulation of the precursor cells and secretion of IFN-γ. The cells are washed away, leaving the secreted IFN bound to the antibody-coated wells in concentrated areas where the cells were sitting. The captured IFN is detected with biotinylated anti-rhesus IFN antibody (detector Ab U-Cytech) followed by alkaline phosphatase-conjugated streptavidin (Pharmingen 13043E). The addition of insoluble alkaline phosphatase substrate results in dark spots in the wells at the sites where the cells were located, leaving one spot for each T cell that secreted IFN-γ.

The number of spots per well is directly related to the precursor frequency of antigen-specific T cells. Gamma interferon was selected as the cytokine visualized in this assay (using species specific anti-gamma interferon monoclonal antibodies) because it is the most common, and one of the most abundant cytokines synthesized and secreted by activated T lymphocytes. For this assay, the number of spot forming cells (SFC) per million PBMCs is determined for samples in the

presence and absence (media control) of peptide antigens. Data from Rhesus macaques on PBMC from post dose two material are shown in Table 4.

Table 4

	PV1J-NSOPTmut		
Pep pools	21G	99C161	99C166
F (NS3p)	8	10	170
G (NS3h)	7	592	229
H (NS4)	3	14	16
I (NS5a)	5	71	36
L (NS5b)	14	23	11
M (NS5b)	3	35	8
DMSO	2	4	5

INFγELISPOT on PBMC from Rhesus monkeys immunized with two injections of 5 mg DNA/dose in OPTIVAX/BAK of plasmid pV1Jns-NSOPTmut. Data are expressed as SFC7 10^6 PBMC.

Example 5: Construction of Ad6 Pre-Adenovirus Plasmids

Ad6 pre-adenovirus plasmids were obtained as follows:

Construction of pAd6 E1-E3+ Pre-adenovirus Plasmid

An Ad6 based pre-adenovirus plasmid which can be used to generate first generation Ad6 vectors was constructed either taking advantage of the extensive sequence identity (approx. 98%) between Ad5 and Ad6 or containing only Ad6 regions. Homologous recombination was used to clone wtAd6 sequences into a bacterial plasmid.

A general strategy used to recover pAd6E1-E3+ as a bacterial plasmid containing Ad5 and Ad6 regions is illustrated in Figure 10. Cotransformation of BJ 5183 bacteria with purified wt Ad6 viral DNA and a second DNA fragment termed the Ad5 ITR cassette resulted in the circularization of the viral genome by homologous recombination. The ITR cassette contains sequences from the right (bp 33798 to 35935) and left (bp 1 to 341 and bp 3525 to 5767) end of the Ad5 genome separated by plasmid sequences containing a bacterial origin of replication and an ampicillin resistance gene. The ITR cassette contains a deletion of E1 sequences from

Ad5 342 to 3524. The Ad5 sequences in the ITR cassette provide regions of homology with the purified Ad6 viral DNA in which recombination can occur.

Potential clones were screened by restriction analysis and one clone was selected as pAd6E1-E3+. This clone was then sequenced in it entirety. pAd6E1-E3+ contains Ad5 sequences from bp 1 to 341 and from bp 3525 to 5548, Ad6 bp 5542 to 33784, and Ad5 bp 33967 to 35935 (bp numbers refer to the wt sequence for both Ad5 and Ad6). pAd6E1-E3+ contains the coding sequences for all Ad6 virion structural proteins which constitute its serotype specificity.

A general strategy used to recover pAd6E1-E3+ as a bacterial plasmid containing Ad6 regions is illustrated in Figure 11. Cotransformation of BJ 5183 bacteria with purified wt Ad6 viral DNA and a second DNA fragment termed the Ad6 ITR cassette resulted in the circularization of the viral genome by homologous recombination. The ITR cassette contains sequences from the right (bp 35460 to 35759) and left (bp 1 to 450 and bp 3508 to 3807) end of the Ad6 genome separated by plasmid sequences containing a bacterial origin of replication and an ampicillin resistance gene. These three segments were generated by PCR and cloned sequentially into pNEB193, generating pNEBAd6-3 (the ITR cassette). The ITR cassette contains a deletion of E1 sequences from Ad5 451 to 3507. The Ad6 sequences in the ITR cassette provide regions of homology with the purified Ad6 viral DNA in which recombination can occur.

Construction of pAd6 E1-E3- pre-adenovirus plasmids

Ad6 based vectors containing A5 regions and deleted in the E3 region were constructed starting with pAd6E1-E3+ containing Ad5 regions. A 5322 bp subfragment of pAd6E1-E3+ containing the E3 region (Ad6 bp 25871 to 31192) was subcloned into pABS.3 generating pABSAd6E3. Three E3 deletions were then made in this plasmid generating three new plasmids pABSAd6E3(1.8Kb) (deleted for Ad6 bp 28602 to 30440), pABSAd6E3(2.3Kb) (deleted for Ad6 bp 28157 to 30437) and pABSAd6E3(2.6Kb) (deleted for Ad6 bp 28157 to 30788). Bacterial recombination was then used to substitute the three E3 deletions back into pAd6E1-E3+ generating the Ad6 genome plasmids pAd6E1-E3-1.8Kb, pAd6E1-E3-2.3Kb and pAd6E1-E3-2.6Kb.

Example 6: Generation of Ad5 Genome Plasmid with the NS Sequence

A pcDNA3 plasmid (Invitrogen) containing the coding region NS3-NS4A-NS4B-NS5A was digested with *Xmn*I and *Nru*I restriction sites and the DNA fragment containing the CMV promoter, the NS3-NS4A-NS4B-NS5A coding sequence and the Bovine Growth Hormone (BGH) polyadenylation signal was cloned into the unique *Eco*rV restriction site of the shuttle vector pDelE1Spa, generating the Sva3-5A vector.

A pcDNA3 plasmid containing the coding region NS3-NS4A-NS4B-NS5A-NS5B was digested with *Xmn*I and *Ecor*I (partial digestion), and the DNA fragment containing part of NS5A, NS5B gene and the BGH polyadenylation signal was cloned into the Sva3-5A vector, digested *Ecor*I and *Bgl*II blunted with Klenow, generating the Sva3-5B vector.

The Sva3-5B vector was finally digested *Ssp*I and *Bst*1107I restriction sites and the DNA fragment containing the expression cassette (CMV promoter, NS3-NS4A-NS4B-NS5A-NS5B coding sequence and the BGH polyadenylation signal) flanked by adenovirus sequences was co-transformed with pAd5HVO (E1-,E3-) ClaI linearized genome plasmid into the bacterial strain BJ5183, to generate pAd5HVONS. pAd5HVO contains Ad5 bp 1 to 341, bp 3525 to 28133 and bp 30818 to 35935.

Example 7: Generation of Adenovirus Genome Plasmids with the NSmut Sequence

Adenovirus genome plasmids containing an NS-mut sequence were generated in an Ad5 or Ad6 background. The Ad6 background contained Ad5 regions at bases 1 to 450, 3511 to 5548 and 33967 to 35935.

pV1JNS3-5Akozak was digested with *Bgl*II and *Xba*I restriction enzymes and the DNA fragment containing the Kozak sequence and the sequence coding NS3-NS4A-NS4B-NS5A was cloned into a *Bgl*II and XbaI digested polypMRKpdelE1 shuttle vector. The resulting vector was designated shNS3-5Akozak.

PolypMRKpdelE1 is a derivative of RKpdelE1(Pac/pIX/pack450) + CMVmin+BGHpA(str.) modified by the insertion of a polylinker containing recognition sites for BglII, PmeI, SwaI, XbaI, SalI, into the unique BglII restriction site present downstream the CMV promoter. MRKpdelE1(Pac/pIX/pack450) + CMVmin + BGHpA(str.) contains Ad5 sequences from bp 1 to 5792 with a deletion of E1 sequences from bp 451 to 3510. The human CMV promoter and BGH polyadenylation signal were inserted into the E1 deletion in an E1 parallel orientation with a unique BglII site separating them.

The NS5B fragment, mutated to abrogate enzymatic activity and with a strong translation termination at the 3' end, was obtained by assembly PCR and inserted into the shNS3-5Akozak vector via homologous recombination, generating polypMRKpdelE1NSmut. In polypMRKpdelE1NSmut the NS-mut coding sequence is under the control of CMV promoter and the BGH polyadenylation signal is present downstream.

The gene expression cassette and the flanking regions which contain adenovirus sequences allowing homologous recombination were excised by digestion with *Pac*I and *Bst*1107I restriction enzymes and co-transformed with either pAd5HVO (E1-,E3-) or pAd6E1-E3-2.6Kb *Cla*I linearized genome plasmids into the bacterial strain BJ5183, to generate pAd5HVONSmut and pAd6E1-,E3-NSmut, respectively.

pAd6E1-E3-2.6Kb contains Ad5 bp 1 to 341 and from bp 3525 to 5548, Ad6 bp 5542 to 28157 and from bp 30788 to 33784, and Ad5 bp 33967 to 35935 (bp numbers refer to the wt sequence for both Ad5 and Ad6). In both plasmids the viral ITR's are joined by plasmid sequences that contain the bacterial origin of replication and an ampicillin resistance gene.

Example 8: Generation of Adenovirus Genome Plasmids with the NSOPTmut

The human codon-optimized synthetic gene (NSOPTmut) provided by SEQ. ID. NO. 3 cloned into a pCRBlunt vector (Invitrogen) was digested with *BamH*1 and *Sal*I restriction enzymes and cloned into *BglII* and *Sal*I restriction sites present in the shuttle vector polypMRKpdelE1. The resulting clone (polypMRKpdelE1NSOPTmut) was digested with *Pac*I and *Bst*1107I restriction enzymes and co-transformed with either pAd5HVO (E1-,E3-) or pAd6E1-E3-2.6Kb *Cla*I linearized genome plasmids, into the bacterial strain BJ5183, to generate pAd5HVONSOPTmut and pAd6E1-,E3-NSOPTmut, respectively.

Example 9: Rescue and Amplification of Adenovirus Vectors

Adenovectors were rescued in Per.6 cells. Per.C6 were grown in 10% FCS / DMEM supplemented by L-glutamine (final 4mM), penicillin/streptomycin (final 100 IU/ml) and 10 mM $MgCl_2$. After infection, cells were kept in the same medium supplemented by 5% horse serum (HS). For viral rescue, 2.5 X 10^6 Per.C6 were plated in 6 cm ø Petri dishes.

Twenty-four hours after plating, cells were transfected by calcium phosphate method with 10 μg of the *Pac I* linearized adenoviral DNA. The DNA precipitate was left on the cells for 4 hours. The medium was removed and 5% HS/DMEM was added.

Cells were kept in a CO_2 incubator until a cytopathic effect was visible (1 week). Cells and supernatant were recovered and subjected to 3X freeze/thawing cycles (liquid nitrogen / water bath at 37^0C). The lysate was centrifuged at 3000 rpm at - 4°C for 20 minutes and the recovered supernatant (corresponding to a cell lysate containing virus passed on cells only once; P1) was used, in the amount of 1 ml/ dish, to infect 80-90% confluent Per.C6 in 10 cm ø Petri dishes. The infected cells were incubated until a cytopathic effect was visible, cells and supernatant recovered and the lysate prepared as described above (P2).

P2 lysate (4 ml) were used to infect 2 X 15 cm ø Petri dishes. The lysate recovered from this infection (P3) was kept in aliquots at –80°C as a stock of virus to be used as starting point for big viral preparations. In this case, 1 ml of the stock was enough to infect 2 X 15 cm ø Petri dishes and resulting lysate (P4) was used for the infection of the Petri dishes devoted to the large scale infection.

Further amplification was obtained from the P4 lysate which was diluted in medium without FCS and used to infect 30 X 15 cm ø Petri dishes (with Per.C6 80%-90% confluent) in the amount of 10 ml/dish. Cells were incubated 1 hour in the CO_2 incubator, mixing gently every 20 minutes. 12 ml / dish of 5% HS / DMEM was added and cells were incubated until a cytopathic effect was visible (about 48 hours).

Cells and supernatant were collected and centrifuged at 2K rpm for 20 minutes at 4^0C. The pellet was resuspended in 15 ml of 0.1 M Tris pH=8.0. Cells were lysed by 3X freeze/thawing cycles (liquid nitrogen / water bath at 37^0C). 150 μl of 2 M $MgCl_2$ and 75 μl of DNAse (10 mg of bovine pancreatic deoxyribonuclease I in 10 ml of 20 mM Tris-HCl pH= 7.4, 50 mM NaCl, 1 mM dithiothreitol, 0.1 mg/ml bovine serum albumin, 50% glycerol) were added. After a 1 hour incubation at 37^0C in a water bath (vortex every 15 minutes) the lysate was centrifuged at 4K rpm for 15 minutes at 4^0C. The recovered supernatant was ready to be applied on CsCl gradient.

The CsCl gradients were prepared in SW40 ultra-clear tubes as follows:

0.5 ml of 1.5d CsCl

3 ml of 1.35d CsCl

3 ml of 1.25d CsCl

5-ml/ tube of viral supernatant was applied.

If necessary, the tubes were topped up with 0.1 M tris-Cl pH=8.0. Tubes were centrifuged at 35K rpm for 1 hour at -10^{0}C with rotor SW40. The viral bands (located at the 1.25/1.35 interface) were collected using a syringe.

The virus was transferred into a new SW40 ultraclear tube and 1.35d CsCl was added to top the tube up. After centrifugation at 35K rpm for 24 hours at 10^{0}C in the rotor SW40, the virus was collected in the smallest possible volume and dialyzed extensively against buffer A105 (5 mM Tris, 5% sucrose, 75 mM NaCl, 1 mM $MgCl_2$, 0.005% polysorbate 80 pH=8.0). After dialysis, glycerol was added to final 10% and the virus was stored in aliquots at – 80^{0}C.

Example 10: Enhanced Adenovector Rescue

First generation Ad5 and Ad6 vectors carrying HCV NSOPTmut transgene were found to be difficult to rescue. A possible block in the rescue process might be attributed to an inefficient replication of plasmid DNA that is a sub-optimal template for the replication machinery of adenovirus. The absence of the terminal protein linked to the 5'ends of the DNA (normally present in the viral DNA), associated with the very high G-C content of the transgene inserted in the E1 region of the vector, may be causing a substantial reduction in replication rate of the plasmid-derived adenovirus.

To set up a more efficient and reproducible procedure for rescuing Ad vectors, an expression vector (pE2; Figure 19) containing all E2 proteins (polymerase, pre-terminal protein and DNA binding protein) as well as E4 orf6 under the control of tet-inducible promoter was employed. The transfection of pE2 in combination with a normal preadeno plasmid in PerC6 and in 293 leads to a strong increase of Ad DNA replication and to a more efficient production of complete infectious adenovirus particles.

Plasmid Construction

pE2 is based on the cloning vector pBI (CLONTECH) with the addition of two elements to allow episomal replication and selection in cell culture: (1) the EBV-OriP (EBV [nt] 7421-8042) region permitting plasmid replication in synchrony with the cell cycle when EBNA-1 is expressed and (2) the hygromycin-B phosphotransferase (HPH)-resistance gene allowing a positive selection of

transformed cells. The two transcriptional units for the adenoviral genes E2 a and b and E4-Orf6 were constructed and assembled in pE2 as described below.

The Ad5-Polymerase *ClaI/SphI* fragment and the Ad5-pTP *Acc65/EcoRV* fragment were obtained from pVac-Pol and pVac-pTP (Stunnemberg *et al. NAR 16*:2431-2444, 1988). Both fragments were filled with Klenow and cloned into the *SalI* (filled) and *EcoRV* sites of pBI, respectively obtaining pBI-Pol/pTP.

EBV-OriP element from pCEP4 (Invitrogen) was first inserted within two chicken β-globin insulator dimers by cloning it into *BamHI* site of pJC13-1 (Chung *et al., Cell 74(3)*:505-14, 1993). HS4-OriP fragment from pJC13-OriP was then cloned inside pSA1mv (a plasmid containing tk-Hygro-B resistance gene expression cassette as well as Ad5 replication origin), the ITR's arranged as head-to-tail junction, obtained by PCR from pFG140 (Graham, *EMBO J. 3*:2917-2922, 1984) using the following primers: 5'-TCGAATCGATACGCGAACCTACGC-3' (SEQ. ID. NO. 16) and 5'-TCGACGTGTCGACTTCGAAGCGCACACCAAAAACGTC-3' (SEQ. ID. NO. 17), thus generating pMVHS4Orip. A DNA fragment from pMVHS4Orip, containing the insulated OriP, Ad5 ITR junction and tk-HygroB cassette, was then inserted into pBI-Pol/pTP vector restricted *AseI/AatII* generating pBI-Pol/pTPHS4 .

To construct the second transcriptional unit expressing Ad5-Orf6 as well as Ad5-DBP, E4orf6 (Ad 5 [nt] 33193-34077) obtained by PCR was first inserted into pBI vector, generating pBI-Orf6. Subsequently, DBP coding DNA sequence (Ad 5 [nt] 22443-24032) was inserted into pBI-Orf6 obtaining the second bi-directional Tet-regulated expression vector (pBI-DBP/E4orf6). The original polyA signals present in pBI were substituted with BGH and SV40 polyA.

pBI-DBP/E4orf6 was then modified by inserting a DNA fragment containing the Adeno5-ITRs arranged in head-to-tail junction plus the hygromicin B resistance gene obtained from plasmid pSA-1mv. The new plasmid pBI-DBP/E4orf6shuttle was then used as donor plasmid to insert the second tet-regulated transcriptional unit into pBI-Pol/pTPHS4 by homologous recombination using *E. coli* strain BJ5183 obtaining pE2.

Cell lines, Transfections and Virus Amplification

PerC6 cells were cultured in Dulbecco's modified Eagle's Medium (DMEM) plus 10% fetal bovine serum (FBS), 10 mM $MgCl_2$, penicillin (100 U/ml), streptomycin (100 μg/ml) and 2 mM glutamine.

All transient transfections were performed using Lipofectamine2000 (Invitrogen) as described by the manufacturer. 90% confluent PERC.6™ planted in 6-cm plates were transfected with 3.5 μg of Ad5/6NSOPTmut pre-adeno plasmids, digested with PacI, alone or in combination with 5 μg pE2 plus 1 μg pUHD52.1. pUHD52.1 is the expression vector for the reverse tet transactivator 2 (rtTA2) (Urlinger *et al., Proc. Natl. Acad. Sci. U.S.A. 97(14)*:7963-7968, 2000). Upon transfection, cells were cultivated in the presence of 1 μg/ml of doxycycline to activate pE2 expression. 7 days post-transfection cells were harvested and cell lysate was obtained by three cycles of freeze-thaw. Two ml of cell lysate were used to infect a second 6-cm dish of PerC6. Infected cells were cultivated until a full CPE was observed then harvested. The virus was serially passaged five times as described above, then purified on CsCl gradient. The DNA structure of the purified virus was controlled by endonuclease digestion and agarose gel electrophoresis analysis and compared to the original pre-adeno plasmid restriction pattern.

<u>Example 11: Partial Optimizeation of HCV Polyprotein Encoding Nucleic acid</u>

Partial optimization of HCV polyprotein encoding nucleic acid was performed to facilitate the production of adenovectors containing codons optimized for expression in a human host. The overall objective was to provide for increased expression due to codon optimization, while facilitating the production of an adenovector encoding HCV polyprotein.

Several difficulties were encountered in producing an adenovector encoding HCV polyprotein with codons optimized for expression in a human host. An adenovector containing an optimized sequence (SEQ. ID. NO. 3) was found to be more difficult to synthesize and rescue than an adenovector containing a non-optimized sequence (SEQ. ID. NO. 2).

The difficulties in producing an adenovector containing SEQ. ID. NO. 3 were attributed to a high GC content. A particularly problemetic region was the region at about position 3900 of NSOPTmut (SEQ. ID. NO. 3).

Alternative versions of optimized HCV encoding nucleic acid sequence were designed to facilitate its use in an adenovector. The alternative versions, compared to NSOPTmut, were designed to have a lower overall GC content, to reduce/avoid the presence of potentially problematic motifs of consecutive G's or C's, while maintaining a high level of codon optimization to allow improved expression of the encoded polyprotein and the individual cleavage products.

A starting point for the generation of a suboptimally codon-optimized sequence is the coding region of the NSOPTmut nucleotide sequence (bases 7 to 5961 of SEQ. ID. NO. 3). Values for codon usage frequencies (normalized to a total of 1.0 for each amino acid) were taken from the file human_high.cod available in the Wisconsin Package Version 10.3 (Accelrys Inc., a wholly owned subsidiary of Pharmacopeia, Inc).

To reduce the local and overall GC content a table defining preferred codon substitutions for each amino acid was manually generated. For each amino acid the codon having 1) a lower GC content as compared to the most frequent codon and 2) a relativly high observed codon usage frequency (as defined in human_high.cod) was choosen as the replacement codon. For example for Arg the codon with the highest frequency is CGC. Out of the other five alternative codons encoding Arg (CGG, AGG, AGA, CGT, CGA) three (AGG, CGT, CGA) reduce the GC content by 1 base, one (AGA) by two bases and one (CGG) by 0 bases. Since the AGA codon is listed in human_high.cod as having a relatively low usage frequency (0.1), the codon substituting CGC was therefore choosen to be AGG with a relative frequency of 0.18. Similar criteria were applied in order to establish codon replacements for the other amino acids resulting in the list shown in Table 5. Parameters applied in the following optimization procedure were determined empirically such that the resulting sequence maintained a considerably improved codon usage (for each amino acid) and the GC content (overall and in form of local stretches of consecutive G's and/or C's) was decreased.

Two examples of partial optimized HCV encoding sequences are provided by SEQ. ID. NO. 10 and SEQ. ID. NO. 11. SEQ. ID. NO. 10 provides a HCV encoding sequence that is partially optimized throughout. SEQ. ID. NO. 11 provides an HCV encoding sequence fully optimized for codon usage with the exception of a region that was partially optimized.

Codon optimization was performed using the following procedure:

Step 1) The coding region of the input fully optimized NSOPTmut sequence was analyzed using a sliding window of 3 codons (9 bases) shifting the window by one codon after each cycle. Whenever a stretch containing 5 or more consecutive C's and/or G's was detected in the window the following replacement rule was applied: Let N indicate the number of codon replacements previously performed. If N is odd replace the middle codon in the window with the codon specified in Table 5, if N is even replace the third terminal codon in the window with the codon

specified in a codon optimization table such as human_high.cod. If Leu or Val is present at the second or third codon do not apply any replacement in order not to introduce Leu or Val codons with very low relative codon usage frequency (see, for example, human_high.cod). In the following cycle analysis of the shifted window was then applied to a sequence containing the replacements of the previous cycle.

The alternating replacement of the middle and terminal codon in the 3 codon window was found empirically to give a more satisfying overall maintenance of optimized codon usage while also reducing GC content (as judged from the final sequence after the procedure). In general, however, the precise replacement strategy depends on the amino acid sequence encoded by the nucelotide sequence under analysis and will have to be determined empirically.

Step 2) The sequence containing all the codon replacements performed during step 1) was then subjected to an additional analysis using a sliding window of 21 codons (63 bases) in length: according to an adjustable parameter the overall GC content in the window was determined. If the GC content in the window was higher than 70% the following codon replacement strategy was applied: In the window replace the codons for the amino acids Asn, Asp, Cys, Glu, His, Ile, Lys, Phe, Tyr by the codons given in Table 5. Restriction of the replacement to this set of amino acids was motivated by the fact that a) the replacement codon still has an accetably high frequency of usage in human_high.cod and b) the average overall human codon usage in CUTG for the replacement codon is nearly as high as the most frequent codon. In the following cycle analysis of the shifted window is then applied to a sequence containing the replacements of the previous cycle.

The threshold 70% was determined empirically by compromising between an overall reduction in GC content and maintenance of a high codon optimization for the individual amino acids. As in step 1) the precise replacement strategy (choice of amino acids and GC content threshold value) will again depend on the amino acid sequence encoded by the nucleotide sequence under analysis and will have to be determined empirically.

Step 3) The sequence generated by steps 1) and 2) was then manually edited and additional codons were changed according to the following criteria: Regions still having a GC content higher than 70% over a window of 21 codons were examined manually and a few codons were replaced again following the scheme given in Table 5.

Subsequent steps were performed to provide for useful restriction sites, remove possible open reading frames on the complementary strand, to add homologous recombinant regions, to add a Kozac signal, and to add a terminator. These steps are numbered 4-7

Step 4) The sequence generated in step 3 was examined for the absence of certain restriction sites (BglII, PmeI and XbaI) and presence of only 1 StuI site to allow a subsequent cloning strategy using a subset of restriction enzymes. Two sites (one for BglII and one for StuI) were removed from the sequence by replacing codons that were part of the respective recognition sites.

Step 5) The sequence generated by steps 1) through 4) was then modified according to allow subsequent generation of a modified NSOPTmut sequence (by homologous recombination). In the sequence obtained from steps 1) through 4) the segment comprising base 3556 to 3755 and the segment comprising base 4456 to 4656 were replaced by the corresponding segments from NSOPTmut. The segment comprising bases 3556 to 4656 of SEQ. ID. NO. 10 can be used to replace the problematic region in NSOPTmut (around position 3900) by homologous recombination thus creating the variant of NSOPTmut having the sequence of SEQ. ID. NO. 11.

Step 6) Analysis of the sequence generated through steps 1) to 5) revealed a potential open reading frame spanning nearly the complete fragment on the complementary strand. Removal of all codons CTA and TTA (Leu) and TCA (Ser) from the sense strand effectively removed all stop codons in one of the reading frames on the complementary strand. Although the likelyhood for transcription of this complementary strand open reading frame and subsequent translation into protein is very small, in order to exclude a potential interference with the transcription and subsequent translation of the sequence encoded on the sense strand, TCA codons for Ser were introduced on the sense approximately every 500 bases. No changes were introduced in the segments introduced during step 5) to allow homologous recombination. The TCA codon for Ser was preferred over the CTA and TTA codons for Leu because of the higher relative frequency for TCA (0.05) as compared to CTA (0.02) and TTA (0.03) in human_high.cod. In addition, the average human codon usage from CUTG favored TCA (0.14 against 0.07 for CTA and TTA).

Step 7) In a final step GCCACC was added at the 5' end of the sequence to generate an optimized internal ribosome entry site (Kozak signal) and a TAAA stop sgnal was added at the 3'. To maintain the initiation of translation

properties of NSsuboptmut the first 8 codons of the coding region were kept identical to the NSOPTmut sequence. The resulting sequence was again checked for the absence of BglII, PmeI and XbaI recognition sites and the presence of only 1 StuI site.

The NSsuboptmut sequence (SEQ. ID. NO. 10) has an overall reduced GC content (63.5%) as compared to NSOPTmut (70.3%) and maintains a well optimized level of codon usage optimization. Nucleotide sequence identity of NSsuboptmut is 77.2% with respect to NSmut.

Table 5: Definition of codon replacements performed during steps 1) and 2).

Amino Acid	Most frequent codon	Relative frequency	Reduction in GC content (bases)	Replacement codon	Relative frequency
Amino Acids where the replacement codon reduces the codon GC-content by 1 base					
Ala	GCC	0.51	1	GCT	0.17
Arg	CGC	0.37	1	AGG	0.18
Asn	AAC	0.78	1	AAT	0.22
Asp	GAC	0.75	1	GAT	0.25
Cys	TGC	0.68	1	TGT	0.32
Glu	GAG	0.75	1	GAA	0.25
Gln	CAG	0.88	1	CAA	0.12
Gly	GGC	0.50	1	GGA	0.14
His	CAC	0.79	1	CAT	0.21
Ile	ATC	0.77	1	ATT	0.18
Lys	AAG	0.82	1	AAA	0.18
Phe	TTC	0.80	1	TTT	0.20
Pro	CCC	0.48	1	CCT	0.19
Ser	AGC	0.34	1	TCT	0.13
Thr	ACC	0.51	1	ACA	0.14
Tyr	TAC	0.74	1	TAT	0.26
Amino Acids with no alternative codon					
Met	ATG	1.00	0	ATG	1.00
Trp	TGG	1.00	0	TGG	1.00

Amino Acids where the replacement codon has a very low relative frequency. These amino acids were excluded from the replacement procedure					
Leu	CTG	0.58	1	TTG	0.06
Val	GTG	0.64	1	GTT	0.07

Example 12: Virus Characterization

Adenovectors were characterized by: (a) measuring the physical particles/ml; (b) running a TaqMan PCR assay; and (c) checking protein expression after infection of HeLa cells.

a) Physical Particles Determination

CsCl purified virus was diluted 1/10 and 1/100 in 0.1% SDS PBS. As a control, buffer A105 was used. These dilutions were incubated 10 minutes at 55^0C. After spinning the tubes briefly, O.D. at 260 nm was measured. The amount of viral particles was calculated as follows: 1 OD 260 nm = 1.1 X 10^{12} physical particles/ml. The results were typically between 5 X 10^{11} and 1 X 10^{12} physical particles /ml.

b) TaqMan PCR Assay

TaqMan PCR assay was used for adenovectors genome quantification (Q-PCR particles/ml). TaqMan PCR assay was performed using the ABI Prism 7700-sequence detector. The reaction was performed in a final 50 μl volume in the presence of oligonucleotides (at final 200 nM) and probe (at final 200 μM) specific for the adenoviral backbone. The virus was diluted 1/10 in 0.1% SDS PBS and incubated 10 minutes at 55^0C. After spinning the tube briefly, serial 1/10 dilutions (in water) were prepared. 10 μl the 10^{-3}, 10^{-5} and 10^{-7} dilutions were used as templates in the PCR assay.

The amount of particles present in each sample was calculated on the basis of a standard curve run in the same experiment. Typically results were between 1 X 10^{12} and 3 X 10^{12} Q-PCR particles /ml.

c) Expression of HCV Non-Structural Proteins

Expression of HCV NS proteins was tested by infection of HeLa cells. Cells were plated the day before the infection at 1.5 X 10^6 cells/dish (10 cm ø Petri dishes). Different amounts of CsCl purified virus corresponding to m.o.i. of 50, 250

and 1250 pp/cell were diluted in medium (FCS free) up to a final volume of 5 ml. The diluted virus was added on the cells and incubated for 1 hour at 37^0C in a CO_2 incubator (gently mixing every 20 minutes). 5 ml of 5% HS-DMEM was added and the cells were incubated at 37^0C for 48 hours.

Cell extracts were prepared in 1% Triton/TEN buffer. The extracts were run on 10% SDS-acrylamide gel, blotted on nitrocellulose and assayed with antibodies directed against NS3, NS5a and NS5b in order to check the correct polyprotein cleavage. Mock-infected cells were used as a negative control. Results from representative experiments testing the Ad5-NS, MRKAd5-NSmut, MRKAd6-NSmut and MRKAd6-NSOPTmut are shown in Figure 14.

Example 13: Mice Immunization with Adenovectors Encoding Different NS Cassettes

The adenovectors Ad5-NS, MRKAd5-NSmut, MRKAd6-NSmut and MRKAd6-NSOPTmut were injected in C57Black6 mice strains to evaluate their potential to elicit anti-HCV immune responses. Groups of animals (N=9-10) were injected intramuscularly with 10^9 pp of CsCl purified virus. Each animal received two doses at three weeks interval.

Humoral immune response against the NS3 protein was measured in post dose two sera from C57Black6 immunized mice by ELISA on bacterially expressed NS3 protease domain. Antibodies specific for the tested antigen were detected with geometric mean titers (GMT) ranging from 100 to 46000 (Tables 6, 7, 8 and 9).

Table 6: Ad5-NS

											GMT
Mice n.	1	2	3	4	5	6	7	8	9	10	
Titer	50	253	50	50	50	2257	504	50	50	50	108

Table 7: Ad5-NSmut

											GMT
Mice n.	11	12	13	14	15	16	17	18	19	20	
Titer	3162	78850	87241	6796	12134	3340	18473	13093	76167	49593	23645

Table 8: MRKAd6-NSmut

											GMT
Mice n.	21	22	23	24	25	26	27	28	29	30	
Titer	125626	39751	40187	65834	60619	69933	21555	49348	29290	26859	46461

Table 9: MRKAd6-NSOPTmut

								GMT
Mice n.	31	32	33	34	35	36	37	
Titer	25430	3657	893	175	10442	49540	173	2785

T cell response in C57Black6 mice was analyzed by the quantitative ELISPOT assay measuring the number of IFNγ secreting T cells in response to five pools (named from F to L+M) of 20mer peptides overlapping by ten residues encompassing the NS3-NS5B sequence. Specific CD8+ response induced in C57Black6 mice was analyzed by the same assay using a 20mer peptide encompassing a CD8+ epitope for C57Black6 mice (pep1480). Cells secreting IFNγ in an antigen specific-manner were detected using a standard ELIspot assay.

Spleen cells, splenocytes and peptides were produced and treated as described in Example 3, *supra*. Representative data from groups of C57Black6 mice (N=9-10) immunized with two injections of 10^9 viral particles of vectors Ad5-NS, MRKAd5-NSmut and MRKAd6-NSmut are shown in Figure 15.

Example 14: Immunization of Rhesus macaques with Adenovectors

Rhesus macaques (N=3-4) were immunized by intramuscular injection of CsCl purified Ad5-NS, MRKAd5-NSmut, MRKAd6-NSmut or MRKAd6-

NSOPTmut virus. Each animal received two doses of 10^{11} or 10^{10} vp in the deltoid muscle at 0, and 4 weeks.

CMI was measured at different time points by a) IFN-γ ELISPOT (see Example 3, *supra*), b) IFN-γ ICS and c) bulk CTL assays. These assays measure HCV antigen-specific CD8+ and CD4+ T lymphocyte responses, and can be used for a variety of mammals, such as humans, rhesus monkeys, mice, and rats.

The use of a specific peptide or a pool of peptides can simplify antigen presentation in CTL cytotoxicity assays, interferon-gamma ELISPOT assays and interferon-gamma intracellular staining assays. Peptides based on the amino acid sequence of various HCV proteins (core, E2, NS3, NS4A, NS4B, NS5a, NS5b) were prepared for use in these assays to measure immune responses in HCV DNA and adenovirus vector vaccinated rhesus monkeys, as well as in HCV-infected humans. The individual peptides are overlapping 20-mers, offset by 10 amino acids. Large pools of peptides can be used to detect an overall response to HCV proteins while smaller pools and individual peptides may be used to define the epitope specificity of a response.

IFN-γ ICS

For IFN-γ ICS, 2 x 10^6 PBMC in 1 ml R10 (RPMI medium, supplemented with 10% FCS) were stimulated with peptide pool antigens. Final concentration of each peptide was 2 μg/ml. Cells were incubated for 1 hour in a CO_2 incubator at 37°C and then Brefeldin A was added to a final concentration of 10 μg /ml to inhibit the secretion of soluble cytokines. Cells were incubated for additional 14-16 hours at 37°C.

Stimulation was done in the presence of co-stimulatory antibodies: CD28 and CD49d (anti-humanCD28 BD340975 and anti-humanCD49d BD340976). After incubation, cells were stained with fluorochrome-conjugated antibodies for surface antigens: anti-CD3, anti-CD4, anti-CD8 (CD3-APC Biosource APS0301, CD4-PE BD345769, CD8-PerCP BD345774).

To detect intracellular cytokines, cells were treated with FACS permeabilization buffer 2 (BD340973), 2x final concentration. Once fixed and permeabilized, cells were incubated with an antibody against human IFN-γ, IFN-γFITC (Biosource AHC4338).

Cells were resuspended in 1% formaldehyde in PBS and analyzed at FACS within 24 hours. Four color FACS analysis was performed on a FACSCalibur

instrument (Becton Dickinson) equipped with two lasers. Acquisition was done gating on the lymphocyte population in the Forward versus Side Scatter plot coupled with the CD3, CD8 positive populations. At least 30,000 events of the gate were taken. The positive cells are expressed as number of IFN-γ expressing cells over 10^6 lymphocytes.

IFN-γ ELISPOT and IFN-γ ICS data from immunized monkeys after one or two injections of 10^{10} or 10^{11} vp of the different adenovectors are reported in Figures 16A-16D, 17A, and 17B.

Bulk CTL Assays

A distinguishing effector function of T lymphocytes is the ability of subsets of this cell population to directly lyse cells exhibiting appropriate MHC-associated antigenic peptides. This cytotoxic activity is most often associated with CD8+ T lymphocytes.

PBMC samples were infected with recombinant vaccine viruses expressing HCV antigens *in vitro* for approximately 14 days to provide antigen restimulation and expansion of memory T cells. Cytotoxicity against autologous B cell lines treated with peptide antigen pools was tested.

The lytic function of the culture is measured as a percentage of specific lysis resulted from chromium released from target cells during 4 hours incubation with CTL effector cells. Specific cytotoxicity is measured and compared to irrelevant antigen or excipient-treated B cell lines. This assay is semi-quantitative and is the preferred means for determining whether CTL responses were elicited by the vaccine. Data after two injections from monkeys immunized with 10^{11} vp/dose with adenovectors Ad5-NS, MRKAd5-NSmut and MRKAd6-NSmut are reported in Figures 18A-18F.

Other embodiments are within the following claims. While several embodiments have been shown and described, various modifications may be made without departing from the spirit and scope of the present invention.

WHAT IS CLAIMED IS:

1. A nucleic acid comprising a nucleotide sequence encoding a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide substantially similar to SEQ ID NO: 1, provided that said polypeptide has sufficient protease activity to process itself to produce an NS5B protein and said NS5B protein is enzymatically inactive.

2. The nucleic acid of claim 1, wherein said nucleotide sequence is substantially similar to the coding sequence of SEQ ID NO: 2.

3. The nucleic acid of claim 1, wherein said nucleotide sequence encodes for the polypeptide of SEQ ID NO: 1.

4. The nucleic acid of claim 3, wherein said nucleotide sequence is the coding sequence of either SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 10, or SEQ ID NO: 11.

5. The nucleic acid of claim 3, wherein said nucleotide sequence is the coding sequence of either SEQ ID NO: 2 or SEQ ID NO: 3.

6. The nucleic acid of any one of claims 1-5, wherein said nucleic acid is an expression vector capable of expressing said polypeptide from said nucleotide sequence in a human cell.

7. A nucleic acid comprising a gene expression cassette able to express a Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide substantially similar to SEQ ID NO: 1 in a human cell, provided that said polypeptide can process itself to produce an NS5B protein and said NS5B protein is enzymatically inactive, said expression cassette comprising:

a) a promoter transcriptionally coupled to a nucleotide sequence encoding said polypeptide;

b) a 5' ribosome binding site functionally coupled to said nucleotide sequence,

c) a terminator joined to the 3' end of said nucleotide sequence, and

d) a 3' polyadenylation signal functionally coupled to said nucleotide sequence.

8. The nucleic acid of claim 7, wherein said nucleotide sequence is substantially similar to either SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 10, or SEQ ID NO: 11.

9. The nucleic acid of claim 8, wherein said nucleic acid is a shuttle vector further comprising a selectable marker, an origin of replication, a first adenovirus homology region and a second adenovirus homology region flanking said expression cassette, wherein said first homology region has at least about 100 base pairs substantially homologous to at least right end of a wild-type adenovirus region from about base pairs 1-425, and said second homology region has at least about 100 base pairs substantially homologous to at least the left end of a wild-type adenovirus region from about base pairs 3511-5792 of Ad5 or corresponding region of another adenovirus.

10. The nucleic acid of claim 9, wherein said nucleotide sequence encodes for a polypeptide of SEQ ID NO: 1.

11. The nucleic acid of claim 9, wherein said nucleotide sequence is SEQ ID NO: 2.

12. The nucleic acid of claim 9, wherein said nucleotide sequence is either SEQ ID NO: 3, SEQ ID NO: 10, or SEQ ID NO: 11.

13. The nucleic acid of claim 8, wherein said nucleic acid is a plasmid suitable for administration into a human and further comprises a prokaryotic origin of replication and a gene coding for a selectable marker.

14. The nucleic acid of claim 13, wherein said nucleotide sequence encodes for a polypeptide of SEQ ID NO: 1.

15. The nucleic acid of claim 14, wherein said nucleotide sequence is the coding sequence of either SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 10, or SEQ ID NO: 11.

16. The nucleic acid of claim 14, wherein said nucleotide sequence is the coding sequence of SEQ ID NO: 2 or SEQ ID NO: 3.

17. The nucleic acid of claim 14, wherein said promoter is the human intermediate early cytomegalovirus promoter (intron A), said 5' ribosome binding site consists of SEQ ID NO: 12, and said 3' polyadenylation is the bovine growth hormone (BGH) polyadenylation signal.

18. The nucleic acid of claim 8, wherein said nucleic acid is a adenovirus genome plasmid comprising a selectable marker, an origin of replication, and a recombinant adenovector genome containing an E1 deletion, an E3 deletion, and said expression cassette.

19. The nucleic acid of claim 8, wherein said nucleic acid is a adenovirus genome plasmid comprising a selectable marker, an origin of replication, and

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) said gene expression cassette in a E1 parallel or E1 anti-parallel orientation joined to said first region;

c) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to said expression cassette;

d) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to said second region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to said third region; and

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to said fourth region.

20. The nucleic acid of claim 19, wherein said first region corresponds to Ad5, said second region corresponds to Ad5, said third region corresponds to Ad5, said fourth region corresponds to Ad5, and said fifth region corresponds to Ad5.

21. The nucleic acid of claim 20, wherein said promoter is the human intermediate early cytomegalovirus promoter, said 5' ribosome binding site consists of SEQ ID NO: 12, and said 3' polyadenylation is the BGH polyadenylation signal.

22. The nucleic acid of claim 21, wherein said expression cassette is in an E1 anti parallel orientation and said nucleotide sequence is either SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 10, or SEQ ID NO: 11.

23. The nucleic acid of claim 19, wherein said first region corresponds to Ad5 or Ad6, said second region corresponds to Ad5 or Ad6, said third region corresponds to Ad6, said fourth region corresponds to Ad6, and said fifth region corresponds to Ad5 or Ad6.

24. The nucleic acid of claim 23, wherein said promoter is the human intermediate early cytomegalovirus promoter, said 5' ribosome binding site consists of SEQ ID NO: 12, and said 3' polyadenylation is the BGH polyadenylation signal.

25. The nucleic acid of claim 24, wherein said expression cassette is in an E1 anti parallel orientation and said nucleotide sequence is either SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 10, or SEQ ID NO: 11.

26. The nucleic acid of claim 24, wherein said expression cassette is in an E1 anti parallel orientation and said nucleotide sequence is either SEQ ID NO: 2 or SEQ ID NO: 3.

27. The nucleic acid of claim 8, wherein said nucleic acid is a adenovirus genome plasmid comprising an origin of replication, a selectable marker, and:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to said first region;

c) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to said second region;

d) said gene expression cassette in a E3 parallel or E3 anti-parallel orientation joined to said third region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to said gene expression cassette; and

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to said fourth region.

28. The nucleic acid of claim 27, wherein said first region corresponds to Ad5, said second region corresponds to Ad5, said third region corresponds to Ad5, said fourth region corresponds to Ad5, and said fifth region corresponds to Ad5.

29. The nucleic acid of claim 28, wherein said promoter is the human intermediate early cytomegalovirus promoter, said 5' ribosome binding site consists of SEQ ID NO: 12, and said 3' polyadenylation is the BGH polyadenylation signal.

30. The nucleic acid of claim 27, wherein said first region corresponds to Ad5 or Ad6, said second region corresponds to Ad5 of Ad6, said third region corresponds to Ad6, said fourth region corresponds to Ad6, and said fifth region corresponds to Ad5 or Ad6.

31. The nucleic acid of claim 30, wherein said promoter is the human intermediate early cytomegalovirus promoter, said 5' ribosome binding site consists of SEQ ID NO: 12, and said 3' polyadenylation is the BGH polyadenylation signal.

32. The nucleic acid of claim 8, wherein said nucleic acid is a adenovector consisting of a nucleotide sequence substantially similar to of SEQ ID NO. 4 or a derivative thereof, wherein said derivative thereof has the HCV polyprotein encoding sequence present in SEQ ID NO: 4 replaced with the HCV polyprotein encoding sequence of either SEQ ID NO: 3, SEQ ID NO: 10 or SEQ ID NO: 11.

33. The nucleic acid of claim 8, wherein said nucleic acid is an adenovector having an adenovector genome containing an E1 deletion, an E3 deletion, and said expression cassette

34. The nucleic acid of claim 8, wherein said nucleic acid is an adenovector consisting of:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) said gene expression cassette in a E1 parallel or E1 anti-parallel orientation joined to said first region;

c) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to said expression cassette;

d) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to said second region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to said third region; and

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to said fourth region.

35. The nucleic acid of claim 34, wherein said first region corresponds to Ad5, said second region corresponds to Ad5, said third region corresponds to Ad5, said fourth region corresponds to Ad5, and said fifth region corresponds to Ad5.

36. The nucleic acid of claim 35, wherein said promoter is the human intermediate early cytomegalovirus promoter, said 5' ribosome binding site consists of SEQ ID NO: 12, and said 3' polyadenylation is the BGH polyadenylation signal.

37. The nucleic acid of claim 36, wherein said expression cassette is in an E1 anti parallel orientation and said nucleotide sequence is either SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 10, or SEQ ID NO: 11.

38. The nucleic acid of claim 34, wherein said first region corresponds to Ad5 or Ad6, said second region corresponds to Ad5 or Ad6, said third region corresponds to Ad6, said fourth region corresponds to Ad6, and said fifth region corresponds to Ad5 or Ad6.

39. The nucleic acid of claim 37, where said promoter is the human intermediate early cytomegalovirus promoter, said 5' ribosome binding site consists of SEQ ID NO: 12, and said 3' polyadenylation is the BGH polyadenylation signal.

40. The nucleic acid of claim 39, wherein said expression cassette is in an E1 anti parallel orientation and said nucleotide sequence is SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 10, or SEQ ID NO: 11.

41. The nucleic acid of claim 39, wherein said expression cassette is in an E1 anti parallel orientation and said nucleotide sequence is SEQ ID NO: 2 or SEQ ID NO: 3.

42. The nucleic acid of claim 8, wherein said nucleic acid is an adenovector consisting of:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to said first region;

c) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to said second region;

d) said gene expression cassette in a E3 parallel or E3 anti-parallel orientation joined to said third region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to said gene expression cassette; and

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to said fourth region.

43. The nucleic acid of claim 42, wherein said first region corresponds to Ad5, said second region corresponds to Ad5, said third region corresponds to Ad5, said fourth region corresponds to Ad5, and said fifth region corresponds to Ad5.

44. The nucleic acid of claim 42, wherein said first region corresponds to Ad5 or Ad6, said second region corresponds to Ad5 or Ad6, said third region corresponds to Ad6, said fourth region corresponds to Ad6, and said fifth region corresponds to Ad5 or Ad6.

45. An adenovector consisting of the nucleic acid sequence of SEQ ID NO. 4 or a derivative thereof, wherein said derivative thereof has the HCV polyprotein encoding sequence present in SEQ ID NO: 4 replaced with the HCV polyprotein encoding sequence of either SEQ ID NO: 3, SEQ ID NO: 10 or SEQ ID NO: 11.

46. An adenovector produced by a process comprising the steps of:

a) producing an adenovirus genome plasmid by homologous recombination between the shuttle vector of claim 9 and a nucleic acid comprising;

a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to said first region;

a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to said second region;

a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to said third region; and

a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to said fourth region; and

b) rescuing said adenovector from said adenovirus plasmid.

47. A cultured recombinant cell comprising the nucleic acid of claim 6.

48. A cultured recombinant cell comprising the nucleic acid of any one of claims 9-46.

49. A method of making an adenovector comprising the steps of:

a) producing an adenovirus genome plasmid comprising a gene expression cassette by homologous recombination between the nucleic acid of claim 9 and a nucleic acid comprising;

a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to said first region;

a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to said second region;

a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to said third region; and

a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to the fourth region; and

b) rescuing said recombinant adenovirus from said recombinant adenovirus plasmid.

50. A pharmaceutical composition comprising the nucleic acid of any one of claims 13-17 and 32-46 and pharmaceutically acceptable carrier.

51. A method of treating a patient comprising the step of administering to said patient an effective amount of the nucleic acid of any one of claims 13-17 and 32-46.

52. The method of claim 51, wherein said patient is a human.

53. The method of claim 52, wherein said patient is not infected with HCV.

54. The method of claim 52, wherein said patient is infected with HCV.

55. A recombinant nucleic acid comprising one or more Ad6 regions and a region not present in Ad6, wherein at least one Ad6 region is selected from the group consisting of: E1A, E1B, E2B, E2A, E4, L1, L2, L4, and L5.

56. The recombinant nucleic acid of claim 55, wherein said region not present in Ad6, is an expression cassette coding for a polypeptide not found in Ad6.

57. The recombinant nucleic acid of claim 56, wherein said recombinant nucleic acid is an adenovirus vector defective in at least E1 that is able to replicate when E1 is supplied *in trans*.

58. The recombinant nucleic acid of claim 57, wherein said vector consists of:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) said gene expression cassette in an E1 parallel or E1 anti-parallel orientation joined to said first region;

c) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to said gene expression cassette;

d) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to said second region;

e) an optionally present fourth region from about base pair 28134 to about base pair 30817 corresponding to Ad5, or from about base pair 28157 to about 30789 corresponding to Ad6, joined to said third region;

f) a fifth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, wherein said fifth region is joined to said fourth region if said fourth region is present, or said fifth is joined to said third region if said fourth region is not present; and

g) a sixth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to said fourth region;

provided that at least one of said second, third, and fifth regions is from Ad6.

59. The recombinant nucleic acid of claim 57, wherein said vector consists of:

a) a first adenovirus region from about base pair 1 to about base pair 450 corresponding to either Ad5 or Ad6;

b) a second adenovirus region from about base pair 3511 to about base pair 5548 corresponding to Ad5 or from about base pair 3508 to about base pair 5541 corresponding to Ad6, joined to said first region;

c) a third adenovirus region from about base pair 5549 to about base pair 28133 corresponding to Ad5 or from about base pair 5542 to about base pair 28156 corresponding to Ad6, joined to said second region;

d) said gene expression cassette in a E3 parallel or E3 anti-parallel orientation joined to said third region;

e) a fourth adenovirus region from about base pair 30818 to about base pair 33966 corresponding to Ad5 or from about base pair 30789 to about base pair 33784 corresponding to Ad6, joined to said gene expression cassette; and

f) a fifth adenovirus region from about base pair 33967 to about base pair 35935 corresponding to Ad5 or from about base pair 33785 to about base pair 35759 corresponding to Ad6, joined to said fourth region;

provided that at least one of said second, third, and fourth regions is from Ad6.

1	MAPITAYSQQ	TRGLLGCIIT	SLTGRDKNQV	EGEVQVVSTA	TQSFLATCVN
51	GVCWTVYHGA	GSKTLAGPKG	PITQMYTNVD	QDLVGWQAPP	GARSLTPCTC
101	GSSDLYLVTR	HADVIPVRRR	GDSRGSLLSP	RPVSYLKGSS	GGPLLCPSGH
151	AVGIFRAAVC	TRGVAKAVDF	VPVESMETTM	RSPVFTDNSS	PPAVPQSFQV
201	AHLHAPTGSG	KSTKVPAAYA	AQGYKVLVLN	PSVAATLGFG	AYMSKAHGID
251	PNIRTGVRTI	TTGAPVTYST	YGKFLADGGC	SGGAYDIIIC	DECHSTDSTT
301	ILGIGTVLDQ	AETAGARLVV	LATATPPGSV	TVPHPNIEEV	ALSNTGEIPF
351	YGKAIPIEAI	RGGRHLIFCH	SKKKCDELAA	KLSGLGINAV	AYYRGLDVSV
401	IPTIGDVVVV	ATDALMTGYT	GDFDSVIDCN	TCVTQTVDFS	LDPTFTIETT
451	TVPQDAVSRS	QRRGRTGRGR	RGIYRFVTPG	ERPSGMFDSS	VLCECYDAGC
501	AWYELTPAET	SVRLRAYLNT	PGLPVCQDHL	EFWESVFTGL	THIDAHFLSQ
551	TKQAGDNFPY	LVAYQATVCA	RAQAPPPSWD	QMWKCLIRLK	PTLHGPTPLL
601	YRLGAVQNEV	TLTHPITKYI	MACMSADLEV	VTSTWVLVGG	VLAALAAYCL
651	TTGSVVIVGR	IILSGRPAIV	PDREFLYQEF	DEMEECASHL	PYIEQGMQLA
701	EQFKQKALGL	LQTATKQAEA	AAPVVESKWR	ALETFWAKHM	WNFISGIQYL
751	AGLSTLPGNP	AIASLMAFTA	SITSPLTTQS	TLLFNILGGW	VAAQLAPPSA
801	ASAFVGAGIA	GAAVGSIGLG	KVLVDILAGY	GAGVAGALVA	FKVMSGEMPS
851	TEDLVNLLPA	ILSPGALVVG	VVCAAILRRH	VGPGEGAVQW	MNRLIAFASR
901	GNHVSPTHYV	PESDAAARVT	QILSSLTITQ	LLKRLHQWIN	EDCSTPCSGS
951	WLRDVWDWIC	TVLTDFKTWL	QSKLLPQLPG	VPFFSCQRGY	KGVWRGDGIM
1001	QTTCPCGAQI	TGHVKNGSMR	IVGPKTCSNT	WHGTFPINAY	TTGPCTPSPA
1051	PNYSRALWRV	AAEEYVEVTR	VGDFHYVTGM	TTDNVKCPCQ	VPAPEFFTEV
1101	DGVRLHRYAP	ACRPLLREEV	TFQVGLNQYL	VGSQLPCEPE	PDVAVLTSML
1151	TDPSHITAET	AKRRLARGSP	PSLASSSASQ	LSAPSLKATC	TTHHVSPDAD
1201	LIEANLLWRQ	EMGGNITRVE	SENKVVVLDS	FDPLRAEEDE	REVSVPAEIL
1251	RKSKKFPAAM	PIWARPDYNP	PLLESWKDPD	YVPPVVHGCP	LPPIKAPPIP
1301	PPRRKRTVVL	TESSVSSALA	ELATKTFGSS	ESSAVDSGTA	TALPDQASDD
1351	GDKGSDVESY	SSMPPLEGEP	GDPDLSDGSW	STVSEEASED	VVCCSMSYTW
1401	TGALITPCAA	EESKLPINAL	SNSLLRHHNM	VYATTSRSAG	LRQKKVTFDR
1451	LQVLDDHYRD	VLKEMKAKAS	TVKAKLLSVE	EACKLTPPHS	AKSKFGYGAK
1501	DVRNLSSKAV	NHIHSVWKDL	LEDTVTPIDT	TIMAKNEVFC	VQPEKGGRKP
1551	ARLIVFPDLG	VRVCEKMALY	DVVSTLPQVV	MGSSYGFQYS	PGQRVEFLVN
1601	TWKSKKNPMG	FSYDTRCFDS	TVTENDIRVE	ESIYQCCDLA	PEARQAIKSL
1651	TERLYIGGPL	TNSKGQNCGY	RRCRASGVLT	TSCGNTLTCY	LKASAACRAA

FIG. 1A

1701	KLQDCTMLVN	AAGLVVICES	AGTQEDAASL	RVFTEAMTRY	SAPPGDPPQP
1751	EYDLELITSC	SSNVSVAHDA	SGKRVYYLTR	DPTTPLARAA	WETARHTPVN
1801	SWLGNIIMYA	PTLWARMILM	THFFSILLAQ	EQLEKALDCQ	IYGACYSIEP
1851	LDLPQIIERL	HGLSAFSLHS	YSPGEINRVA	SCLRKLGVPP	LRVWRHRARS
1901	VRARLLSQGG	RAATCGKYLF	NWAVKTKLKL	TPIPAASQLD	LSGWFVAGYS
1951	GGDIYHSLSR	ARPRWFMLCL	LLLSVGVGIY	LLPNR	

FIG. 1B

1	GCCACCATGG	CGCCCATCAC	GGCCTACTCC	CAACAGACGC	GGGGCCTACT
51	TGGTTGCATC	ATCACTAGCC	TTACAGGCCG	GGACAAGAAC	CAGGTCGAGG
101	GAGAGGTTCA	GGTGGTTTCC	ACCGCAACAC	AATCCTTCCT	GGCGACCTGC
151	GTCAACGGCG	TGTGTTGGAC	CGTTTACCAT	GGTGCTGGCT	CAAAGACCTT
201	AGCCGGCCCA	AAGGGGCCAA	TCACCCAGAT	GTACACTAAT	GTGGACCAGG
251	ACCTCGTCGG	CTGGCAGGCG	CCCCCCGGGG	CGCGTTCCTT	GACACCATGC
301	ACCTGTGGCA	GCTCAGACCT	TTACTTGGTC	ACGAGACATG	CTGACGTCAT
351	TCCGGTGCGC	CGGCGGGGCG	ACAGTAGGGG	GAGCCTGCTC	TCCCCCAGGC
401	CTGTCTCCTA	CTTGAAGGGC	TCTTCGGGTG	GTCCACTGCT	CTGCCCTTCG
451	GGGCACGCTG	TGGGCATCTT	CCGGGCTGCC	GTATGCACCC	GGGGGGTTGC
501	GAAGGCGGTG	GACTTTGTGC	CCGTAGAGTC	CATGGAAACT	ACTATGCGGT
551	CTCCGGTCTT	CACGGACAAC	TCATCCCCCC	CGGCCGTACC	GCAGTCATTT
601	CAAGTGGCCC	ACCTACACGC	TCCCACTGGC	AGCGGCAAGA	GTACTAAAGT
651	GCCGGCTGCA	TATGCAGCCC	AAGGGTACAA	GGTGCTCGTC	CTCAATCCGT
701	CCGTTGCCGC	TACCTTAGGG	TTTGGGGCGT	ATATGTCTAA	GGCACACGGT
751	ATTGACCCCA	ACATCAGAAC	TGGGGTAAGG	ACCATTACCA	CAGGCGCCCC
801	CGTCACATAC	TCTACCTATG	GCAAGTTTCT	TGCCGATGGT	GGTTGCTCTG
851	GGGGCGCTTA	TGACATCATA	ATATGTGATG	AGTGCCATTC	AACTGACTCG
901	ACTACAATCT	TGGGCATCGG	CACAGTCCTG	GACCAAGCGG	AGACGGCTGG
951	AGCGCGGCTT	GTCGTGCTCG	CCACCGCTAC	GCCTCCGGGA	TCGGTCACCG
1001	TGCCACACCC	AAACATCGAG	GAGGTGGCCC	TGTCTAATAC	TGGAGAGATC
1051	CCCTTCTATG	GCAAAGCCAT	CCCCATTGAA	GCCATCAGGG	GGGGAAGGCA
1101	TCTCATTTTC	TGTCATTCCA	AGAAGAAGTG	CGACGAGCTC	GCCGCAAAGC
1151	TGTCAGGCCT	CGGAATCAAC	GCTGTGGCGT	ATTACCGGGG	GCTCGATGTG
1201	TCCGTCATAC	CAACTATCGG	AGACGTCGTT	GTCGTGGCAA	CAGACGCTCT
1251	GATGACGGGC	TATACGGGCG	ACTTTGACTC	AGTGATCGAC	TGTAACACAT
1301	GTGTCACCCA	GACAGTCGAC	TTCAGCTTGG	ATCCCACCTT	CACCATTGAG
1351	ACGACGACCG	TGCCTCAAGA	CGCAGTGTCG	CGCTCGCAGC	GGCGGGGTAG
1401	GACTGGCAGG	GGTAGGAGAG	GCATCTACAG	GTTTGTGACT	CCGGGAGAAC
1451	GGCCCTCGGG	CATGTTCGAT	TCCTCGGTCC	TGTGTGAGTG	CTATGACGCG
1501	GGCTGTGCTT	GGTACGAGCT	CACCCCCGCC	GAGACCTCGG	TTAGGTTGCG
1551	GGCCTACCTG	AACACACCAG	GGTTGCCCGT	TTGCCAGGAC	CACCTGGAGT
1601	TCTGGGAGAG	TGTCTTCACA	GGCCTCACCC	ACATAGATGC	ACACTTCTTG
1651	TCCCAGACCA	AGCAGGCAGG	AGACAACTTC	CCCTACCTGG	TAGCATACCA

FIG. 2A

1701	AGCCACGGTG	TGCGCCAGGG	CTCAGGCCCC	ACCTCCATCA	TGGGATCAAA
1751	TGTGGAAGTG	TCTCATACGG	CTGAAACCTA	CGCTGCACGG	GCCAACACCC
1801	TTGCTGTACA	GGCTGGGAGC	CGTCCAAAAT	GAGGTCACCC	TCACCCACCC
1851	CATAACCAAA	TACATCATGG	CATGCATGTC	GGCTGACCTG	GAGGTCGTCA
1901	CTAGCACCTG	GGTGCTGGTG	GGCGGAGTCC	TTGCAGCTCT	GGCCGCGTAT
1951	TGCCTGACAA	CAGGCAGTGT	GGTCATTGTG	GGTAGGATTA	TCTTGTCCGG
2001	GAGGCCGGCT	ATTGTTCCCG	ACAGGGAGTT	TCTCTACCAG	GAGTTCGATG
2051	AAATGGAAGA	GTGCGCCTCG	CACCTCCCTT	ACATCGAGCA	GGGAATGCAG
2101	CTCGCCGAGC	AATTCAAGCA	GAAAGCGCTC	GGGTTACTGC	AAACAGCCAC
2151	CAAACAAGCG	GAGGCTGCTG	CTCCCGTGGT	GGAGTCCAAG	TGGCGAGCCC
2201	TTGAGACATT	CTGGGCGAAG	CACATGTGGA	ATTTCATCAG	CGGGATACAG
2251	TACTTAGCAG	GCTTATCCAC	TCTGCCTGGG	AACCCCGCAA	TAGCATCATT
2301	GATGGCATTC	ACAGCCTCTA	TCACCAGCCC	GCTCACCACC	CAAAGTACCC
2351	TCCTGTTTAA	CATCTTGGGG	GGGTGGGTGG	CTGCCCAACT	CGCCCCCCCC
2401	AGCGCCGCTT	CGGCTTTCGT	GGGCGCCGGC	ATCGCCGGTG	CGGCTGTTGG
2451	CAGCATAGGC	CTTGGGAAGG	TGCTTGTGGA	CATTCTGGCG	GGTTATGGAG
2501	CAGGAGTGGC	CGGCGCGCTC	GTGGCCTTCA	AGGTCATGAG	CGGCGAGATG
2551	CCCTCCACCG	AGGACCTGGT	CAATCTACTT	CCTGCCATCC	TCTCTCCTGG
2601	CGCCCTGGTC	GTCGGGGTCG	TGTGTGCAGC	AATACTGCGT	CGACACGTGG
2651	GTCCGGGAGA	GGGGGCTGTG	CAGTGGATGA	ACCGGCTGAT	AGCGTTCGCC
2701	TCGCGGGGTA	ATCATGTTTC	CCCCACGCAC	TATGTGCCTG	AGAGCGACGC
2751	CGCAGCGCGT	GTTACTCAGA	TCCTCTCCAG	CCTTACCATC	ACTCAGCTGC
2801	TGAAAAGGCT	CCACCAGTGG	ATTAATGAAG	ACTGCTCCAC	ACCGTGTTCC
2851	GGCTCGTGGC	TAAGGGATGT	TTGGGACTGG	ATATGCACGG	TGTTGACTGA
2901	CTTCAAGACC	TGGCTCCAGT	CCAAGCTCCT	GCCGCAGCTA	CCGGGAGTCC
2951	CTTTTTTCTC	GTGCCAACGC	GGGTACAAGG	GAGTCTGGCG	GGGAGACGGC
3001	ATCATGCAAA	CCACCTGCCC	ATGTGGAGCA	CAGATCACCG	GACATGTCAA
3051	AAACGGTTCC	ATGAGGATCG	TCGGGCCTAA	GACCTGCAGC	AACACGTGGC
3101	ATGGAACATT	CCCCATCAAC	GCATACACCA	CGGGCCCCTG	CACACCCTCT
3151	CCAGCGCCAA	ACTATTCTAG	GGCGCTGTGG	CGGGTGGCCG	CTGAGGAGTA
3201	CGTGGAGGTC	ACGCGGGTGG	GGGATTTCCA	CTACGTGACG	GGCATGACCA
3251	CTGACAACGT	AAAGTGCCCA	TGCCAGGTTC	CGGCTCCTGA	ATTCTTCACG
3301	GAGGTGGACG	GAGTGCGGTT	GCACAGGTAC	GCTCCGGCGT	GCAGGCCTCT
3351	CCTACGGGAG	GAGGTTACAT	TCCAGGTCGG	GCTCAACCAA	TACCTGGTTG

FIG. 2B

3401	GGTCACAGCT	ACCATGCGAG	CCCGAACCGG	ATGTAGCAGT	GCTCACTTCC
3451	ATGCTCACCG	ACCCCTCCCA	CATCACAGCA	GAAACGGCTA	AGCGTAGGTT
3501	GGCCAGGGGG	TCTCCCCCCT	CCTTGGCCAG	CTCTTCAGCT	AGCCAGTTGT
3551	CTGCGCCTTC	CTTGAAGGCG	ACATGCACTA	CCCACCATGT	CTCTCCGGAC
3601	GCTGACCTCA	TCGAGGCCAA	CCTCCTGTGG	CGGCAGGAGA	TGGGCGGGAA
3651	CATCACCCGC	GTGGAGTCGG	AGAACAAGGT	GGTAGTCCTG	GACTCTTTCG
3701	ACCCGCTTCG	AGCGGAGGAG	GATGAGAGGG	AAGTATCCGT	TCCGGCGGAG
3751	ATCCTGCGGA	AATCCAAGAA	GTTCCCCGCA	GCGATGCCCA	TCTGGGCGCG
3801	CCCGGATTAC	AACCCTCCAC	TGTTAGAGTC	CTGGAAGGAC	CCGGACTACG
3851	TCCCTCCGGT	GGTGCACGGG	TGCCCGTTGC	CACCTATCAA	GGCCCCTCCA
3901	ATACCACCTC	CACGGAGAAA	GAGGACGGTT	GTCCTAACAG	AGTCCTCCGT
3951	GTCTTCTGCC	TTAGCGGAGC	TCGCTACTAA	GACCTTCGGC	AGCTCCGAAT
4001	CATCGGCCGT	CGACAGCGGC	ACGGCGACCG	CCCTTCCTGA	CCAGGCCTCC
4051	GACGACGGTG	ACAAAGGATC	CGACGTTGAG	TCGTACTCCT	CCATGCCCCC
4101	CCTTGAGGGG	GAACCGGGGG	ACCCCGATCT	CAGTGACGGG	TCTTGGTCTA
4151	CCGTGAGCGA	GGAAGCTAGT	GAGGATGTCG	TCTGCTGCTC	AATGTCCTAC
4201	ACATGGACAG	GCGCCTTGAT	CACGCCATGC	GCTGCGGAGG	AAAGCAAGCT
4251	GCCCATCAAC	GCGTTGAGCA	ACTCTTTGCT	GCGCCACCAT	AACATGGTTT
4301	ATGCCACAAC	ATCTCGCAGC	GCAGGCCTGC	GGCAGAAGAA	GGTCACCTTT
4351	GACAGACTGC	AAGTCCTGGA	CGACCACTAC	CGGGACGTGC	TCAAGGAGAT
4401	GAAGGCGAAG	GCGTCCACAG	TTAAGGCTAA	ACTCCTATCC	GTAGAGGAAG
4451	CCTGCAAGCT	GACGCCCCCA	CATTCGGCCA	AATCCAAGTT	TGGCTATGGG
4501	GCAAAGGACG	TCCGGAACCT	ATCCAGCAAG	GCCGTTAACC	ACATCCACTC
4551	CGTGTGGAAG	GACTTGCTGG	AAGACACTGT	GACACCAATT	GACACCACCA
4601	TCATGGCAAA	AAATGAGGTT	TTCTGTGTCC	AACCAGAGAA	AGGAGGCCGT
4651	AAGCCAGCCC	GCCTTATCGT	ATTCCCAGAT	CTGGGAGTCC	GTGTATGCGA
4701	GAAGATGGCC	CTCTATGATG	TGGTCTCCAC	CCTTCCTCAG	GTCGTGATGG
4751	GCTCCTCATA	CGGATTCCAG	TACTCTCCTG	GGCAGCGAGT	CGAGTTCCTG
4801	GTGAATACCT	GGAAATCAAA	GAAAAACCCC	ATGGGCTTTT	CATATGACAC
4851	TCGCTGTTTC	GACTCAACGG	TCACCGAGAA	CGACATCCGT	GTTGAGGAGT
4901	CAATTTACCA	ATGTTGTGAC	TTGGCCCCCG	AAGCCAGACA	GGCCATAAAA
4951	TCGCTCACAG	AGCGGCTTTA	TATCGGGGGT	CCTCTGACTA	ATTCAAAAGG
5001	GCAGAACTGC	GGTTATCGCC	GGTGCCGCGC	GAGCGGCGTG	CTGACGACTA
5051	GCTGCGGTAA	CACCCTCACA	TGTTACTTGA	AGGCCTCTGC	AGCCTGTCGA

FIG. 2C

5101 GCTGCGAAGC TCCAGGACTG CACGATGCTC GTGAACGCCG CCGGCCTTGT
5151 CGTTATCTGT GAAAGCGCGG GAACCCAAGA GGACGCGGCG AGCCTACGAG
5201 TCTTCACGGA GGCTATGACT AGGTACTCTG CCCCCCCCGG GGACCCGCCC
5251 CAACCAGAAT ACGACTTGGA GCTGATAACA TCATGTTCCT CCAATGTGTC
5301 GGTCGCCCAC GATGCATCAG GCAAAAGGGT GTACTACCTC ACCCGTGATC
5351 CCACCACCCC CCTCGCACGG GCTGCGTGGG AAACAGCTAG ACACACTCCA
5401 GTTAACTCCT GGCTAGGCAA CATTATCATG TATGCGCCCA CTTTGTGGGC
5451 AAGGATGATT CTGATGACTC ACTTCTTCTC CATCCTTCTA GCACAGGAGC
5501 AACTTGAAAA AGCCCTGGAC TGCCAGATCT ACGGGGCCTG TTACTCCATT
5551 GAGCCACTTG ACCTACCTCA GATCATTGAA CGACTCCATG GCCTTAGCGC
5601 ATTTTCACTC CATAGTTACT CTCCAGGTGA GATCAATAGG GTGGCTTCAT
5651 GCCTCAGGAA ACTTGGGGTA CCACCCTTGC GAGTCTGGAG ACATCGGGCC
5701 AGGAGCGTCC GCGCTAGGCT ACTGTCCCAG GGGGGGAGGG CCGCCACTTG
5751 TGGCAAGTAC CTCTTCAACT GGGCAGTGAA GACCAAACTC AAACTCACTC
5801 CAATCCCGGC TGCGTCCCAG CTGGACTTGT CCGGCTGGTT CGTTGCTGGT
5851 TACAGCGGGG GAGACATATA TCACAGCCTG TCTCGTGCCC GACCCCGCTG
5901 GTTCATGCTG TGCCTACTCC TACTTTCTGT AGGGGTAGGC ATCTACCTGC
5951 TCCCCAACCG ATAAA

FIG. 2D

1	GCCACCATGG	CCCCCATCAC	CGCCTACAGC	CAGCAGACCC	GCGGCCTGCT
51	GGGCTGCATC	ATCACCAGCC	TGACCGGCCG	CGACAAGAAC	CAGGTGGAGG
101	GCGAGGTGCA	GGTGGTGAGC	ACCGCCACCC	AGAGCTTCCT	GGCCACCTGC
151	GTGAACGGCG	TGTGCTGGAC	CGTGTACCAC	GGCGCCGGCA	GCAAGACCCT
201	GGCCGGCCCC	AAGGGCCCCA	TCACCCAGAT	GTACACCAAC	GTGGACCAGG
251	ACCTGGTGGG	CTGGCAGGCC	CCCCCCGGCG	CCCGCAGCCT	GACCCCCTGC
301	ACCTGCGGCA	GCAGCGACCT	GTACCTGGTG	ACCCGCCACG	CCGACGTGAT
351	CCCCGTGCGC	CGCCGCGGCG	ACAGCCGCGG	CAGCCTGCTG	AGCCCCCGCC
401	CCGTGAGCTA	CCTGAAGGGC	AGCAGCGGCG	GCCCCCTGCT	GTGCCCCAGC
451	GGCCACGCCG	TGGGCATCTT	CCGCGCCGCC	GTGTGCACCC	GCGGCGTGGC
501	CAAGGCCGTG	GACTTCGTGC	CCGTGGAGAG	CATGGAGACC	ACCATGCGCA
551	GCCCCGTGTT	CACCGACAAC	AGCAGCCCCC	CCGCCGTGCC	CCAGAGCTTC
601	CAGGTGGCCC	ACCTGCACGC	CCCCACCGGC	AGCGGCAAGA	GCACCAAGGT
651	GCCCGCCGCC	TACGCCGCCC	AGGGCTACAA	GGTGCTGGTG	CTGAACCCCA
701	GCGTGGCCGC	CACCCTGGGC	TTCGGCGCCT	ACATGAGCAA	GGCCCACGGC
751	ATCGACCCCA	ACATCCGCAC	CGGCGTGCGC	ACCATCACCA	CCGGCGCCCC
801	CGTGACCTAC	AGCACCTACG	GCAAGTTCCT	GGCCGACGGC	GGCTGCAGCG
851	GCGGCGCCTA	CGACATCATC	ATCTGCGACG	AGTGCCACAG	CACCGACAGC
901	ACCACCATCC	TGGGCATCGG	CACCGTGCTG	GACCAGGCCG	AGACCGCCGG
951	CGCCCGCCTG	GTGGTGCTGG	CCACCGCCAC	CCCCCCCGGC	AGCGTGACCG
1001	TGCCCCACCC	CAACATCGAG	GAGGTGGCCC	TGAGCAACAC	CGGCGAGATC
1051	CCCTTCTACG	GCAAGGCCAT	CCCCATCGAG	GCCATCCGCG	GCGGCCGCCA
1101	CCTGATCTTC	TGCCACAGCA	AGAAGAAGTG	CGACGAGCTG	GCCGCCAAGC
1151	TGAGCGGCCT	GGGCATCAAC	GCCGTGGCCT	ACTACCGCGG	CCTGGACGTG
1201	AGCGTGATCC	CCACCATCGG	CGACGTGGTG	GTGGTGGCCA	CCGACGCCCT
1251	GATGACCGGC	TACACCGGCG	ACTTCGACAG	CGTGATCGAC	TGCAACACCT
1301	GCGTGACCCA	GACCGTGGAC	TTCAGCCTGG	ACCCCACCTT	CACCATCGAG
1351	ACCACCACCG	TGCCCCAGGA	CGCCGTGAGC	CGCAGCCAGC	GCCGCGGCCG
1401	CACCGGCCGC	GGCCGCCGCG	GCATCTACCG	CTTCGTGACC	CCCGGCGAGC
1451	GCCCCAGCGG	CATGTTCGAC	AGCAGCGTGC	TGTGCGAGTG	CTACGACGCC
1501	GGCTGCGCCT	GGTACGAGCT	GACCCCCGCC	GAGACCAGCG	TGCGCCTGCG
1551	CGCCTACCTG	AACACCCCCG	GCCTGCCCGT	GTGCCAGGAC	CACCTGGAGT
1601	TCTGGGAGAG	CGTGTTCACC	GGCCTGACCC	ACATCGACGC	CCACTTCCTG
1651	AGCCAGACCA	AGCAGGCCGG	CGACAACTTC	CCCTACCTGG	TGGCCTACCA

FIG. 3A

```
1701  GGCCACCGTG TGCGCCCGCG CCCAGGCCCC CCCCCCCAGC TGGGACCAGA
1751  TGTGGAAGTG CCTGATCCGC CTGAAGCCCA CCCTGCACGG CCCCACCCCC
1801  CTGCTGTACC GCCTGGGCGC CGTGCAGAAC GAGGTGACCC TGACCCACCC
1851  CATCACCAAG TACATCATGG CCTGCATGAG CGCCGACCTG GAGGTGGTGA
1901  CCAGCACCTG GGTGCTGGTG GGCGGCGTGC TGGCCGCCCT GGCCGCCTAC
1951  TGCCTGACCA CCGGCAGCGT GGTGATCGTG GGCCGCATCA TCCTGAGCGG
2001  CCGCCCCGCC ATCGTGCCCG ACCGCGAGTT CCTGTACCAG GAGTTCGACG
2051  AGATGGAGGA GTGCGCCAGC CACCTGCCCT ACATCGAGCA GGGCATGCAG
2101  CTGGCCGAGC AGTTCAAGCA GAAGGCCCTG GGCCTGCTGC AGACCGCCAC
2151  CAAGCAGGCC GAGGCCGCCG CCCCCGTGGT GGAGAGCAAG TGGCGCGCCC
2201  TGGAGACCTT CTGGGCCAAG CACATGTGGA ACTTCATCAG CGGCATCCAG
2251  TACCTGGCCG GCCTGAGCAC CCTGCCCGGC AACCCCGCCA TCGCCAGCCT
2301  GATGGCCTTC ACCGCCAGCA TCACCAGCCC CCTGACCACC CAGAGCACCC
2351  TGCTGTTCAA CATCCTGGGC GGCTGGGTGG CCGCCCAGCT GGCCCCCCCC
2401  AGCGCCGCCA GCGCCTTCGT GGGCGCCGGC ATCGCCGGCG CCGCCGTGGG
2451  CAGCATCGGC CTGGGCAAGG TGCTGGTGGA CATCCTGGCC GGCTACGGCG
2501  CCGGCGTGGC CGGCGCCCTG GTGGCCTTCA AGGTGATGAG CGGCGAGATG
2551  CCCAGCACCG AGGACCTGGT GAACCTGCTG CCCGCCATCC TGAGCCCCGG
2601  CGCCCTGGTG GTGGGCGTGG TGTGCGCCGC CATCCTGCGC CGCCACGTGG
2651  GCCCCGGCGA GGGCGCCGTG CAGTGGATGA ACCGCCTGAT CGCCTTCGCC
2701  AGCCGCGGCA ACCACGTGAG CCCCACCCAC TACGTGCCCG AGAGCGACGC
2751  CGCCGCCCGC GTGACCCAGA TCCTGAGCAG CCTGACCATC ACCCAGCTGC
2801  TGAAGCGCCT GCACCAGTGG ATCAACGAGG ACTGCAGCAC CCCCTGCAGC
2851  GGCAGCTGGC TGCGCGACGT GTGGGACTGG ATCTGCACCG TGCTGACCGA
2901  CTTCAAGACC TGGCTGCAGA GCAAGCTGCT GCCCCAGCTG CCCGGCGTGC
2951  CCTTCTTCAG CTGCCAGCGC GGCTACAAGG GCGTGTGGCG CGGCGACGGC
3001  ATCATGCAGA CCACCTGCCC CTGCGGCGCC CAGATCACCG GCCACGTGAA
3051  GAACGGCAGC ATGCGCATCG TGGGCCCCAA GACCTGCAGC AACACCTGGC
3101  ACGGCACCTT CCCCATCAAC GCCTACACCA CCGGCCCCTG CACCCCCAGC
3151  CCCGCCCCCA ACTACAGCCG CGCCCTGTGG CGCGTGGCCG CCGAGGAGTA
3201  CGTGGAGGTG ACCCGCGTGG GCGACTTCCA CTACGTGACC GGCATGACCA
3251  CCGACAACGT GAAGTGCCCC TGCCAGGTGC CCGCCCCCGA GTTCTTCACC
3301  GAGGTGGACG GCGTGCGCCT GCACCGCTAC GCCCCCGCCT GCCGCCCCCT
3351  GCTGCGCGAG GAGGTGACCT TCCAGGTGGG CCTGAACCAG TACCTGGTGG
```

FIG. 3B

3401	GCAGCCAGCT	GCCCTGCGAG	CCCGAGCCCG	ACGTGGCCGT	GCTGACCAGC
3451	ATGCTGACCG	ACCCCAGCCA	CATCACCGCC	GAGACCGCCA	AGCGCCGCCT
3501	GGCCCGCGGC	AGCCCCCCCA	GCCTGGCCAG	CAGCAGCGCC	AGCCAGCTGA
3551	GCGCCCCCAG	CCTGAAGGCC	ACCTGCACCA	CCCACCACGT	GAGCCCCGAC
3601	GCCGACCTGA	TCGAGGCCAA	CCTGCTGTGG	CGCCAGGAGA	TGGGCGGCAA
3651	CATCACCCGC	GTGGAGAGCG	AGAACAAGGT	GGTGGTGCTG	GACAGCTTCG
3701	ACCCCCTGCG	CGCCGAGGAG	GACGAGCGCG	AGGTGAGCGT	GCCCGCCGAG
3751	ATCCTGCGCA	AGAGCAAGAA	GTTCCCCGCC	GCCATGCCCA	TCTGGGCCCG
3801	CCCCGACTAC	AACCCCCCCC	TGCTGGAGAG	CTGGAAGGAC	CCCGACTACG
3851	TGCCCCCCGT	GGTGCACGGC	TGCCCCCTGC	CCCCCATCAA	GGCCCCCCCC
3901	ATCCCCCCCC	CCCGCCGCAA	GCGCACCGTG	GTGCTGACCG	AGAGCAGCGT
3951	GAGCAGCGCC	CTGGCCGAGC	TGGCCACCAA	GACCTTCGGC	AGCAGCGAGA
4001	GCAGCGCCGT	GGACAGCGGC	ACCGCCACCG	CCCTGCCCGA	CCAGGCCAGC
4051	GACGACGGCG	ACAAGGGCAG	CGACGTGGAG	AGCTACAGCA	GCATGCCCCC
4101	CCTGGAGGGC	GAGCCCGGCG	ACCCCGACCT	GAGCGACGGC	AGCTGGAGCA
4151	CCGTGAGCGA	GGAGGCCAGC	GAGGACGTGG	TGTGCTGCAG	CATGAGCTAC
4201	ACCTGGACCG	GCGCCCTGAT	CACCCCCTGC	GCCGCCGAGG	AGAGCAAGCT
4251	GCCCATCAAC	GCCCTGAGCA	ACAGCCTGCT	GCGCCACCAC	AACATGGTGT
4301	ACGCCACCAC	CAGCCGCAGC	GCCGGCCTGC	GCCAGAAGAA	GGTGACCTTC
4351	GACCGCCTGC	AGGTGCTGGA	CGACCACTAC	CGCGACGTGC	TGAAGGAGAT
4401	GAAGGCCAAG	GCCAGCACCG	TGAAGGCCAA	GCTGCTGAGC	GTGGAGGAGG
4451	CCTGCAAGCT	GACCCCCCCC	CACAGCGCCA	AGAGCAAGTT	CGGCTACGGC
4501	GCCAAGGACG	TGCGCAACCT	GAGCAGCAAG	GCCGTGAACC	ACATCCACAG
4551	CGTGTGGAAG	GACCTGCTGG	AGGACACCGT	GACCCCCATC	GACACCACCA
4601	TCATGGCCAA	GAACGAGGTG	TTCTGCGTGC	AGCCCGAGAA	GGGCGGCCGC
4651	AAGCCCGCCC	GCCTGATCGT	GTTCCCCGAC	CTGGGCGTGC	GCGTGTGCGA
4701	GAAGATGGCC	CTGTACGACG	TGGTGAGCAC	CCTGCCCCAG	GTGGTGATGG
4751	GCAGCAGCTA	CGGCTTCCAG	TACAGCCCCG	GCCAGCGCGT	GGAGTTCCTG
4801	GTGAACACCT	GGAAGAGCAA	GAAGAACCCC	ATGGGCTTCA	GCTACGACAC
4851	CCGCTGCTTC	GACAGCACCG	TGACCGAGAA	CGACATCCGC	GTGGAGGAGA
4901	GCATCTACCA	GTGCTGCGAC	CTGGCCCCCG	AGGCCCGCCA	GGCCATCAAG
4951	AGCCTGACCG	AGCGCCTGTA	CATCGGCGGC	CCCCTGACCA	ACAGCAAGGG
5001	CCAGAACTGC	GGCTACCGCC	GCTGCCGCGC	CAGCGGCGTG	CTGACCACCA
5051	GCTGCGGCAA	CACCCTGACC	TGCTACCTGA	AGGCCAGCGC	CGCCTGCCGC

FIG. 3C

5101 GCCGCCAAGC TGCAGGACTG CACCATGCTG GTGAACGCCG CCGGCCTGGT
5151 GGTGATCTGC GAGAGCGCCG GCACCCAGGA GGACGCCGCC AGCCTGCGCG
5201 TGTTCACCGA GGCCATGACC CGCTACAGCG CCCCCCCCGG CGACCCCCCC
5251 CAGCCCGAGT ACGACCTGGA GCTGATCACC AGCTGCAGCA GCAACGTGAG
5301 CGTGGCCCAC GACGCCAGCG GCAAGCGCGT GTACTACCTG ACCCGCGACC
5351 CCACCACCCC CCTGGCCCGC GCCGCCTGGG AGACCGCCCG CCACACCCCC
5401 GTGAACAGCT GGCTGGGCAA CATCATCATG TACGCCCCCA CCCTGTGGGC
5451 CCGCATGATC CTGATGACCC ACTTCTTCAG CATCCTGCTG GCCCAGGAGC
5501 AGCTGGAGAA GGCCCTGGAC TGCCAGATCT ACGGCGCCTG CTACAGCATC
5551 GAGCCCCTGG ACCTGCCCCA GATCATCGAG CGCCTGCACG GCCTGAGCGC
5601 CTTCAGCCTG CACAGCTACA GCCCCGGCGA GATCAACCGC GTGGCCAGCT
5651 GCCTGCGCAA GCTGGGCGTG CCCCCCCTGC GCGTGTGGCG CCACCGCGCC
5701 CGCAGCGTGC GCGCCCGCCT GCTGAGCCAG GGCGGCCGCG CCGCCACCTG
5751 CGGCAAGTAC CTGTTCAACT GGGCCGTGAA GACCAAGCTG AAGCTGACCC
5801 CCATCCCCGC CGCCAGCCAG CTGGACCTGA GCGGCTGGTT CGTGGCCGGC
5851 TACAGCGGCG GCGACATCTA CCACAGCCTG AGCCGCGCCC GCCCCCGCTG
5901 GTTCATGCTG TGCCTGCTGC TGCTGAGCGT GGGCGTGGGC ATCTACCTGC
5951 TGCCCAACCG CTAAA

FIG. 3D

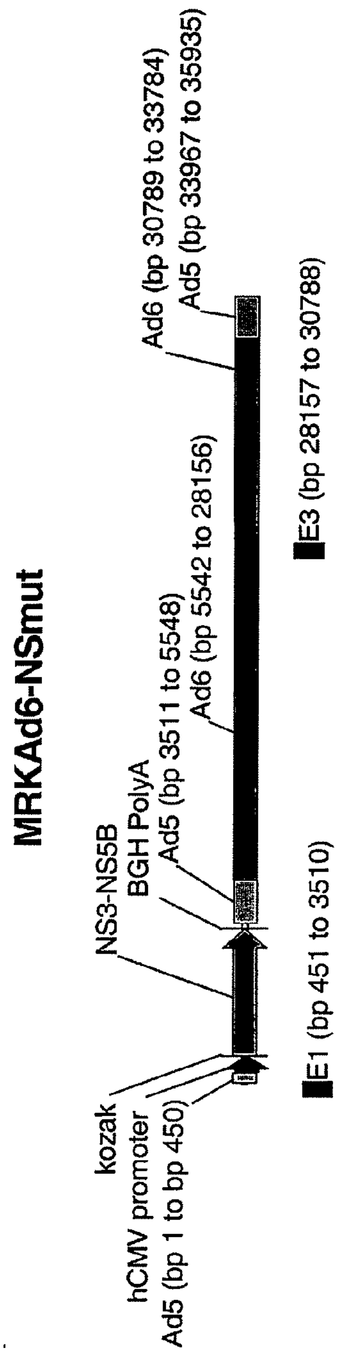

MRKAd6-NSmut
kozak
hCMV promoter
Ad5 (bp 1 to bp 450)
NS3-NS5B
BGH PolyA
Ad5 (bp 3511 to 5548)
Ad6 (bp 5542 to 28156)
Ad6 (bp 30789 to 33784)
Ad5 (bp 33967 to 35935)
E1 (bp 451 to 3510)
E3 (bp 28157 to 30788)

FIG. 4A

```
   1 catcatcaat aatatacctt attttggatt gaagccaata tgataatgag ggggtggagt
  61 ttgtgacgtg gcgcggggcg tgggaacggg gcgggtgacg tagtagtgtg gcggaagtgt
 121 gatgttgcaa gtgtggcgga acacatgtaa gcgacggatg tggcaaaagt gacgtttttg
 181 gtgtgcgccg gtgtacacag gaagtgacaa ttttcgcgcg gttttaggcg gatgttgtag
 241 taaatttggg cgtaaccgag taagatttgg ccattttcgc gggaaaactg aataagagga
 301 agtgaaatct gaataatttt gtgttactca tagcgcgtaa tatttgtcta gggccgcggg
 361 gactttgacc gtttacgtgg agactcgccc aggtgttttt ctcaggtgtt ttccgcgttc
 421 cgggtcaaag ttggcgtttt attattatag gcggccgcga tccattgcat acgttgtatc
 481 catatcataa tatgtacatt tatattggct catgtccaac attaccgcca tgttgacatt
 541 gattattgac tagttattaa tagtaatcaa ttacggggtc attagttcat agcccatata
 601 tggagttccg cgttacataa cttacggtaa atggcccgcc tggctgaccg cccaacgacc
 661 cccgcccatt gacgtcaata atgacgtatg ttcccatagt aacgccaata gggactttcc
 721 attgacgtca atgggtggag tatttacggt aaactgccca cttggcagta catcaagtgt
 781 atcatatgcc aagtacgccc cctattgacg tcaatgacgg taaatggccc gcctggcatt
 841 atgcccagta catgacctta tgggactttc ctacttggca gtacatctac gtattagtca
 901 tcgctattac catggtgatg cggttttggc agtacatcaa tgggcgtgga tagcggtttg
 961 actcacgggg atttccaagt ctccacccca ttgacgtcaa tgggagtttg ttttggcacc
1021 aaaatcaacg ggactttcca aaatgtcgta acaactccgc cccattgacg caaatgggcg
1081 gtaggcgtgt acggtgggag gtctatataa gcagagctcg tttagtgaac cgtcagatcg
1141 cctggagacg ccatccacgc tgttttgacc tccatagaag acaccgggac cgatccagcc
1201 tccgcggccg ggaacggtgc attggaacgc ggattccccg tgccaagagt gagatctgcc
1261 accatggcgc ccatcacggc ctactcccaa cagacgcggg gcctacttgg ttgcatcatc
1321 actagcctta caggccggga caagaaccag gtcgagggag aggttcaggt ggtttccacc
1381 gcaacacaat ccttcctggc gacctgcgtc aacggcgtgt gttggaccgt ttaccatggt
1441 gctggctcaa agaccttagc cggcccaaag ggccaatca cccagatgta cactaatgtg
1501 gaccaggacc tcgtcggctg gcaggcgccc cccgggcgc gttccttgac accatgcacc
1561 tgtggcagct cagaccttta cttggtcacg agacatgctg acgtcattcc ggtgcgccgg
1621 cggggcgaca gtagggggag cctgctctcc cccaggcctg tctcctactt gaagggctct
1681 tcgggtggtc cactgctctg cccttcgggg cacgctgtgg gcatcttccg ggctgccgta
1741 tgcacccggg gggttgcgaa ggcggtggac tttgtgcccg tagagtccat ggaaactact
1801 atgcggtctc cggtcttcac ggacaactca tcccccccgg ccgtaccgca gtcatttcaa
1861 gtggcccacc tacacgctcc cactggcagc ggcaagagta ctaaagtgcc ggctgcatat
1921 gcagcccaag ggtacaaggt gctcgtcctc aatccgtccg ttgccgctac cttagggttt
1981 ggggcgtata tgtctaaggc acacggtatt gaccccaaca tcagaactgg ggtaaggacc
2041 attaccacag gcgcccccgt cacatactct acctatggca agtttcttgc cgatggtggt
2101 tgctctgggg gcgcttatga catcataata tgtgatgagt gccattcaac tgactcgact
2161 acaatcttgg gcatcggcac agtcctggac caagcggaga cggctggagc gcggcttgtc
2221 gtgctcgcca ccgctacgcc tccgggatcg gtcaccgtgc cacacccaaa catcgaggag
2281 gtggccctgt ctaatactgg agagatcccc ttctatggca aagccatccc cattgaagcc
2341 atcagggggg gaaggcatct cattttctgt cattccaaga agaagtgcga cgagctcgcc
2401 gcaaagctgt caggcctcgg aatcaacgct gtggcgtatt accgggggct cgatgtgtcc
2461 gtcataccaa ctatcggaga cgtcgttgtc gtggcaacag acgctctgat gacgggctat
2521 acgggcgact ttgactcagt gatcgactgt aacacatgtg tcacccagac agtcgacttc
2581 agcttggatc ccaccttcac cattgagacg acgaccgtgc ctcaagacgc agtgtcgcgc
2641 tcgcagcggc ggggtaggac tggcaggggt aggagaggca tctacaggtt tgtgactccg
2701 ggagaacggc cctcgggcat gttcgattcc tcggtcctgt gtgagtgcta tgacgcgggc
2761 tgtgcttggt acgagctcac ccccgccgag acctcggtta ggttgcgggc ctacctgaac
2821 acaccagggt tgcccgtttg ccaggaccac ctggagttct gggagagtgt cttcacaggc
2881 ctcacccaca tagatgcaca cttcttgtcc cagaccaagc aggcaggaga caacttcccc
2941 tacctggtag cataccaagc cacggtgtgc gccagggctc aggccccacc tccatcatgg
3001 gatcaaatgt ggaagtgtct catacggctg aaacctacgc tgcacgggcc aacacccttg
3061 ctgtacaggc tgggagccgt ccaaaatgag gtcaccctca cccaccccat aaccaaatac
3121 atcatggcat gcatgtcggc tgacctggag gtcgtcacta gcacctgggt gctggtgggc
3181 ggagtccttg cagctctggc cgcgtattgc ctgacaacag gcagtgtggt cattgtgggt
3241 aggattatct tgtccgggag gccggctatt gttcccgaca gggagtttct ctaccaggag
```

FIG. 4B

3361 gccgagcaat tcaagcagaa agcgctcggg ttactgcaaa cagccaccaa acaagcggag
3421 gctgctgctc ccgtggtgga gtccaagtgg cgagcccttg agacattctg ggcgaagcac
3481 atgtggaatt tcatcagcgg gatacagtac ttagcaggct tatccactct gcctgggaac
3541 cccgcaatag catcattgat ggcattcaca gcctctatca ccagcccgct caccacccaa
3601 agtaccctcc tgtttaacat cttggggggg tgggtggctg cccaactcgc cccccccagc
3661 gccgcttcgg ctttcgtggg cgccggcatc gccggtgcgg ctgttggcag cataggcctt
3721 gggaaggtgc ttgtggacat tctggcgggt tatggagcag gagtggccgg cgcgctcgtg
3781 gccttcaagg tcatgagcgg cgagatgccc tccaccgagg acctggtcaa tctacttcct
3841 gccatcctct ctcctggcgc cctggtcgtc ggggtcgtgt gtgcagcaat actgcgtcga
3901 cacgtgggtc cgggagaggg ggctgtgcag tggatgaacc ggctgatagc gttcgcctcg
3961 cggggtaatc atgtttcccc cacgcactat gtgcctgaga gcgacgccgc agcgcgtgtt
4021 actcagatcc tctccagcct taccatcact cagctgctga aaaggctcca ccagtggatt
4081 aatgaagact gctccacacc gtgttccggc tcgtggctaa gggatgtttg ggactggata
4141 tgcacggtgt tgactgactt caagacctgg ctccagtcca agctcctgcc gcagctaccg
4201 ggagtccctt ttttctcgtg ccaacgcggg tacaagggag tctggcgggg agacggcatc
4261 atgcaaacca cctgcccatg tggagcacag atcaccggac atgtcaaaaa cggttccatg
4321 aggatcgtcg ggcctaagac ctgcagcaac acgtggcatg gaacattccc catcaacgca
4381 tacaccacgg gcccctgcac accctctcca gcgccaaact attctagggc gctgtggcgg
4441 gtggccgctg aggagtacgt ggaggtcacg cgggtggggg atttccacta cgtgacgggc
4501 atgaccactg acaacgtaaa gtgcccatgc caggttccgg ctcctgaatt cttcacggag
4561 gtggacggag tgcggttgca caggtacgct ccggcgtgca ggcctctcct acgggaggag
4621 gttacattcc aggtcgggct caaccaatac ctggttgggt cacagctacc atgcgagccc
4681 gaaccggatg tagcagtgct cacttccatg ctcaccgacc cctcccacat cacagcagaa
4741 acggctaagc gtaggttggc caggggggtct cccccctcct tggccagctc ttcagctagc
4801 cagttgtctg cgccttcctt gaaggcgaca tgcactaccc accatgtctc tccggacgct
4861 gacctcatcg aggccaacct cctgtggcgg caggagatgg gcgggaacat cacccgcgtg
4921 gagtcggaga acaaggtggt agtcctggac tctttcgacc cgcttcgagc ggaggaggat
4981 gagagggaag tatccgttcc ggcggagatc ctgcggaaat ccaagaagtt ccccgcagcg
5041 atgcccatct gggcgcgccc ggattacaac cctccactgt tagagtcctg gaaggacccg
5101 gactacgtcc ctccggtggt gcacgggtgc ccgttgccac ctatcaaggc ccctccaata
5161 ccacctccac ggagaaagag gacggttgtc ctaacagagt cctccgtgtc ttctgcctta
5221 gcggagctcg ctactaagac cttcggcagc tccgaatcat cggccgtcga cagcggcacg
5281 gcgaccgccc ttcctgacca ggcctccgac gacggtgaca aaggatccga cgttgagtcg
5341 tactcctcca tgcccccccct tgagggggaa ccgggggacc ccgatctcag tgacgggtct
5401 tggtctaccg tgagcgagga agctagtgag gatgtcgtct gctgctcaat gtcctacaca
5461 tggacaggcg ccttgatcac gccatgcgct gcggaggaaa gcaagctgcc catcaacgcg
5521 ttgagcaact ctttgctgcg ccaccataac atggtttatg ccacaacatc tcgcagcgca
5581 ggcctgcggc agaagaaggt cacctttgac agactgcaag tcctggacga ccactaccgg
5641 gacgtgctca aggagatgaa ggcgaaggcg tccacagtta aggctaaact cctatccgta
5701 gaggaagcct gcaagctgac gcccccacat tcggccaaat ccaagtttgg ctatggggca
5761 aaggacgtcc ggaacctatc cagcaaggcc gttaaccaca tccactccgt gtggaaggac
5821 ttgctggaag acactgtgac accaattgac accaccatca tggcaaaaaa tgaggttttc
5881 tgtgtccaac cagagaaagg aggccgtaag ccagcccgcc ttatcgtatt cccagatctg
5941 ggagtccgtg tatgcgagaa gatggccctc tatgatgtgg tctccaccct tcctcaggtc
6001 gtgatgggct cctcatacgg attccagtac tctcctgggc agcgagtcga gttcctggtg
6061 aatacctgga aatcaaagaa aaaccccatg ggcttttcat atgacactcg ctgtttcgac
6121 tcaacggtca ccgagaacga catccgtgtt gaggagtcaa tttaccaatg ttgtgacttg
6181 gcccccgaag ccagacaggc cataaaatcg ctcacagagc ggctttatat cgggggtcct
6241 ctgactaatt caaaagggca gaactgcggt tatcgccggt gccgcgcgag cggcgtgctg
6301 acgactagct gcggtaacac cctcacatgt tacttgaagg cctctgcagc ctgtcgagct
6361 gcgaagctcc aggactgcac gatgctcgtg aacgccgccg gccttgtcgt tatctgtgaa
6421 agcgcgggaa cccaagagga cgcggcgagc ctacgagtct tcacggaggc tatgactagg
6481 tactctgccc cccccgggga cccgccccaa ccagaatacg acttggagct gataacatca
6541 tgttcctcca atgtgtcggt cgcccacgat gcatcaggca aaagggtgta ctacctcacc
6601 cgtgatccca ccaccccccct cgcacgggct gcgtgggaaa cagctagaca cactccagtt

FIG. 4C

6661 aactcctggc taggcaacat tatcatgtat gcgcccactt tgtgggcaag gatgattctg
6721 atgactcact tcttctccat ccttctagca caggagcaac ttgaaaaagc cctggactgc
6781 cagatctacg ggcctgtta ctccattgag ccacttgacc tacctcagat cattgaacga
6841 ctccatggcc ttagcgcatt ttcactccat agttactctc caggtgagat caatagggtg
6901 gcttcatgcc tcaggaaact tggggtacca ccccttgcgag tctggagaca tcgggccagg
6961 agcgtccgcg ctaggctact gtcccagggg gggagggccg ccacttgtgg caagtacctc
7021 ttcaactggg cagtgaagac caaactcaaa ctcactccaa tcccggctgc gtcccagctg
7081 gacttgtccg gctggttcgt tgctggttac agcgggggag acatatatca cagcctgtct
7141 cgtgcccgac cccgctggtt catgctgtgc ctactcctac tttctgtagg ggtaggcatc
7201 tacctgctcc ccaaccggta aatctagagc tgtgccttct agttgccagc catctgttgt
7261 ttgcccctcc cccgtgcctt ccttgaccct ggaaggtgcc actcccactg tcctttccta
7321 ataaaatgag gaaattgcat cgcattgtct gagtaggtgt cattctattc tggggggtgg
7381 ggtggggcag gacagcaagg gggaggattg ggaagacaat agcaggcatg ctggggatgc
7441 ggtgggctct atggccgatc ggcgcgccgt actgaaatgt gtgggcgtgg cttaagggtg
7501 ggaaagaata tataaggtgg gggtcttatg tagttttgta tctgttttgc agcagccgcc
7561 gccgccatga gcaccaactc gtttgatgga agcattgtga gctcatattt gacaacgcgc
7621 atgcccccat gggccggggt gcgtcagaat gtgatgggct ccagcattga tggtcgcccc
7681 gtcctgcccg caaactctac taccttgacc tacgagaccg tgtctggaac gccgttggag
7741 actgcagcct ccgccgccgc ttcagccgct gcagccaccg cccgcgggat tgtgactgac
7801 tttgctttcc tgagcccgct tgcaagcagt gcagcttccc gttcatccgc ccgcgatgac
7861 aagttgacgg ctcttttggc acaattggat tctttgaccc gggaacttaa tgtcgtttct
7921 cagcagctgt tggatctgcg ccagcaggtt tctgccctga aggcttcctc ccctcccaat
7981 gcggtttaaa acataaataa aaaaccagac tctgtttgga tttggatcaa gcaagtgtct
8041 tgctgtcttt atttaggggt tttgcgcgcg cggtaggccc gggaccagcg gtctcggtcg
8101 ttgagggtcc tgtgtatttt ttccaggacg tggtaaaggt gactctggat gttcagatac
8161 atgggcataa gcccgtctct ggggtggagg tagcaccact gcagagcttc atgctgcggg
8221 gtggtgttgt agatgatcca gtcgtagcag gagcgctggg cgtggtgcct aaaaatgtct
8281 ttcagtagca agctgattgc caggggcagg cccttggtgt aagtgtttac aaagcggtta
8341 agctgggatg ggtgcatacg tggggatatg agatgcatct tggactgtat ttttaggttg
8401 gctatgttcc cagccatatc cctccgggga ttcatgttgt gcagaaccac cagcacagtg
8461 tatccggtgc acttgggaaa tttgtcatgt agcttagaag gaaatgcgtg gaagaacttg
8521 gagacgccct tgtgacctcc aagattttcc atgcattcgt ccataatgat ggcaatgggc
8581 ccacgggcgg cggcctgggc gaagatattt ctgggatcac taacgtcata gttgtgttcc
8641 aggatgagat cgtcataggc catttttaca aagcgcgggc ggagggtgcc agactgcggt
8701 ataatggttc catccggccc aggggcgtag ttaccctcac agatttgcat ttcccacgct
8761 ttgagttcag atggggggat catgtctacc tgcggggcga tgaagaaaac ggtttccggg
8821 gtaggggaga tcagctggga agaaagcagg ttcctgagca gctgcgactt accgcagccg
8881 gtgggcccgt aaatcacacc tattaccggc tgcaactggt agttaagaga gctgcagctg
8941 ccgtcatccc tgagcagggg ggccacttcg ttaagcatgt ccctgactcg catgttttcc
9001 ctgaccaaat ccgccagaag gcgctcgccg cccagcgata gcagttcttg caaggaagca
9061 aagtttttca acggtttgag accgtccgcc gtaggcatgc ttttgagcgt ttgaccaagc
9121 agttccaggc ggtcccacag ctcggtcacc tgctctacgg catctcgatc cagcatatct
9181 cctcgtttcg cgggttgggg cggctttcgc tgtacggcag tagtcggtgc tcgtccagac
9241 gggccagggt catgtctttc cacgggcgca gggtcctcgt cagcgtagtc tgggtcacgg
9301 tgaaggggtg cgctccgggc tgcgcgctgg ccagggtgcg cttgaggctg gtcctgctgg
9361 tgctgaagcg ctgccggtct tcgccctgcg cgtcggccag gtagcatttg accatggtgt
9421 catagtccag cccctccgcg gcgtggccct tggcgcgcag cttgcccttg gaggaggcgc
9481 cgcacgaggg gcagtgcaga cttttgaggg cgtagagctt gggcgcgaga aataccgatt
9541 ccggggagta ggcatccgcg ccgcaggccc cgcagacggt ctcgcattcc acgagccagg
9601 tgagctctgg ccgttcgggg tcaaaaacca ggtttccccc atgctttttg atgcgtttct
9661 tacctctggt ttccatgagc cggtgtccac gctcggtgac gaaaaggctg tccgtgtccc
9721 cgtatacaga cttgagaggc ctgtcctcga gcggtgttcc gcggtcctcc tcgtatagaa
9781 actcggacca ctctgagacg aaggctcgcg tccaggccag cacgaaggag gctaagtggg
9841 aggggtagcg gtcgttgtcc actagggggt ccactcgctc cagggtgtga agacacatgt
9901 cgccctcttc ggcatcaagg aaggtgattg gtttataggt gtaggccacg tgaccgggtg

FIG. 4D

9961 ttcctgaagg ggggctataa aagggggtgg gggcgcgttc gtcctcactc tcttccgcat
10021 cgctgtctgc gagggccagc tgttggggtg agtactccct ctcaaaagcg ggcatgactt
10081 ctgcgctaag attgtcagtt tccaaaaacg aggaggattt gatattcacc tggcccgcgg
10141 tgatgccttt gagggtggcc gcgtccatct ggtcagaaaa gacaatcttt ttgttgtcaa
10201 gcttggtggc aaacgacccg tagagggcgt tggacagcaa cttggcgatg gagcgcaggg
10261 tttggttttt gtcgcgatcg gcgcgctcct tggccgcgat gtttagctgc acgtattcgc
10321 gcgcaacgca ccgccattcg ggaaagacgg tggtgcgctc gtcgggcact aggtgcacgc
10381 gccaaccgcg gttgtgcagg gtgacaaggt caacgctggt ggctacctct ccgcgtaggc
10441 gctcgttggt ccagcagagg cggccgccct tgcgcgagca gaatggcggt agtgggtcta
10501 gctgcgtctc gtccgggggg tctgcgtcca cggtaaagac cccgggcagc aggcgcgcgt
10561 cgaagtagtc tatcttgcat ccttgcaagt ctagcgcctg ctgccatgcg cgggcggcaa
10621 gcgcgcgctc gtatgggttg agtgggggac cccatggcat ggggtgggtg agcgcggagg
10681 cgtacatgcc gcaaatgtcg taaacgtaga ggggctctct gagtattcca agatatgtag
10741 ggtagcatct tccaccgcgg atgctggcgc gcacgtaatc gtatagttcg tgcgagggag
10801 cgaggaggtc gggaccgagg ttgctacggg cgggctgctc tgctcggaag actatctgcc
10861 tgaagatggc atgtgagttg gatgatatgg ttggacgctg gaagacgttg aagctggcgt
10921 ctgtgagacc taccgcgtca cgcacgaagg aggcgtagga gtcgcgcagc ttgttgacca
10981 gctcggcggt gacctgcacg tctagggcgc agtagtccag ggtttccttg atgatgtcat
11041 acttatcctg tccctttttt ttccacagct cgcggttgag gacaaactct tcgcggtctt
11101 tccagtactc ttggatcgga aacccgtcgg cctccgaacg gtaagagcct agcatgtaga
11161 actggttgac ggcctggtag gcgcagcatc ccttttctac gggtagcgcg tatgcctgcg
11221 cggccttccg gagcgaggtg tgggtgagcg caaaggtgtc cctaaccatg actttgaggt
11281 actggtattt gaagtcagtg tcgtcgcatc cgccctgctc ccagagcaaa aagtccgtgc
11341 gctttttgga acgcgggttt ggcagggcga aggtgacatc gttgaagagt atctttcccg
11401 cgcgaggcat aaagttgcgt gtgatgcgga agggtcccgg cacctcggaa cggttgttaa
11461 ttacctgggc ggcgagcacg atctcgtcaa agccgttgat gttgtggccc acaatgtaaa
11521 gttccaagaa gcgcgggatg cccttgatgg aaggcaattt tttaagttcc tcgtaggtga
11581 gctcttcagg ggagctgagc ccgtgctctg aaagggccca gtctgcaaga tgagggttgg
11641 aagcgacgaa tgagctccac aggtcacggg ccattagcat ttgcaggtgg tcgcgaaagg
11701 tcctaaactg gcgacctatg gccatttttt ctggggtgat gcagtagaag gtaagcgggt
11761 cttgttccca gcggtcccat ccaaggtccg cggctaggtc tcgcgcggcg gtcactagag
11821 gctcatctcc gccgaacttc atgaccagca tgaagggcac gagctgcttc ccaaaggccc
11881 ccatccaagt ataggtctct acatcgtagg tgacaaagag acgctcggtg cgaggatgcg
11941 agccgatcgg gaagaactgg atctcccgcc accagttgga ggagtggctg ttgatgtggt
12001 gaaagtagaa gtccctgcga cggccgaac actcgtgctg gcttttgtaa aaacgtgcgc
12061 agtactggca gcggtgcacg ggctgtacat cctgcacgag gttgacctga cgaccgcgca
12121 caaggaagca gagtgggaat ttgagcccct cgcctggcgg gtttggctgg tggtcttcta
12181 cttcggctgc ttgtccttga ccgtctggct gctcgagggg agttacggtg gatcggacca
12241 ccacgccgcg cgagcccaaa gtccagatgt ccgcgcgcgg cggtcggagc ttgatgacaa
12301 catcgcgcag atgggagctg tccatggtct ggagctcccg cggcgtcagg tcaggcggga
12361 gctcctgcag gtttacctcg catagccggg tcagggcgcg ggctaggtcc aggtgatacc
12421 tgatttccag gggctggttg gtggcggcgt cgatggcttg caagaggccg catccccgcg
12481 gcgcgactac ggtaccgcgc ggcgggcggt gggccgcggg ggtgtccttg gatgatgcat
12541 ctaaaagcgg tgacgcgggc gggcccccgg aggtaggggg ggctcgggac ccgccgggag
12601 agggggcagg ggcacgtcgg cgccgcgcgc gggcaggagc tggtgctgcg cgcggaggtt
12661 gctggcgaac gcgacgacgc ggcggttgat ctcctgaatc tggcgcctct gcgtgaagac
12721 gacgggcccg gtgagcttga acctgaaaga gagttcgaca gaatcaattt cggtgtcgtt
12781 gacggcggcc tggcgcaaaa tctcctgcac gtctcctgag ttgtcttgat aggcgatctc
12841 ggccatgaac tgctcgatct cttcctcctg gagatctccg cgtccggctc gctccacggt
12901 ggcggcgagg tcgttggaga tgcgggccat gagctgcgag aaggcgttga ggcctccctc
12961 gttccagacg cggctgtaga ccacgccccc ttcggcatcg cgggcgcgca tgaccacctg
13021 cgcgagattg agctccacgt gccgggcgaa gacggcgtag tttcgcaggc gctgaaagag
13081 gtagttgagg gtggtggcgg tgtgttctgc cacgaagaag tacataaccc agcgccgcaa
13141 cgtggattcg ttgatatccc ccaaggcctc aaggcgctcc atggcctcgt agaagtccac
13201 ggcgaagttg aaaaactggg agttgcgcgc cgacacggtt aactcctcct ccagaagacg

FIG. 4E

13261 gatgagctcg gcgacagtgt cgcgcacctc gcgctcaaag gctacagggg cctcttcttc
13321 ttcttcaatc tcctcttcca taagggcctc cccttcttct tcttctggcg gcggtggggg
13381 aggggggaca cggcggcgac gacggcgcac cgggaggcgg tcgacaaagc gctcgatcat
13441 ctccccgcgg cgacggcgca tggtctcggt gacggcgcgg ccgttctcgc gggggcgcag
13501 ttggaagacg ccgcccgtca tgtcccggtt atgggttggc ggggggctgc cgtgcggcag
13561 ggatacggcg ctaacgatgc atctcaacaa ttgttgtgta ggtactccgc caccgaggga
13621 cctgagcgag tccgcatcga ccggatcgga aaacctctcg agaaaggcgt ctaaccagtc
13681 acagtcgcaa ggtaggctga gcaccgtggc gggcggcagc gggcggcggt cggggttgtt
13741 tctggcggag gtgctgctga tgatgtaatt aaagtaggcg gtcttgagac ggcggatggt
13801 cgacagaagc accatgtcct tgggtccggc ctgctgaatg cgcaggcggt cggccatgcc
13861 ccaggcttcg ttttgacatc ggcgcaggtc tttgtagtag tcttgcatga gcctttctac
13921 cggcacttct tcttctcctt cctcttgtcc tgcatctctt gcatctatcg ctgcggcggc
13981 ggcggagttt ggccgtaggt ggcgccctct tcctcccatg cgtgtgaccc cgaagcccct
14041 catcggctga agcagggcca ggtcggcgac aacgcgctcg gctaatatgg cctgctgcac
14101 ctgcgtgagg gtagactgga agtcgtccat gtccacaaag cggtggtatg cgcccgtgtt
14161 gatggtgtaa gtgcagttgg ccataacgga ccagttaacg gtctggtgac ccggctgcga
14221 gagctcggtg tacctgagac gcgagtaagc ccttgagtca aagacgtagt cgttgcaagt
14281 ccgcaccagg tactggtatc ccaccaaaaa gtgcggcggc ggctggcggt agaggggcca
14341 gcgtagggtg gccggggctc cgggggcgag gtcttccaac ataaggcgat gatatccgta
14401 gatgtacctg gacatccagg tgatgccggc ggcggtggtg gaggcgcgcg gaaagtcacg
14461 gacgcggttc cagatgttgc gcagcggcaa aaagtgctcc atggtcggga cgctctggcc
14521 ggtcaggcgc gcgcagtcgt tgacgctcta gaccgtgcaa aaggagagcc tgtaagcggg
14581 cactcttccg tggtctggtg gataaattcg caagggtatc atggcggacg accggggttc
14641 gaaccccgga tccggccgtc cgccgtgatc catgcggtta ccgcccgcgt gtcgaaccca
14701 ggtgtgcgac gtcagacaac gggggagcgc tcctttggc ttccttccag gcgcggcgga
14761 tgctgcgcta gcttttttgg ccactggccg cgcgcggcgt aagcggttag gctggaaagc
14821 gaaagcatta agtggctcgc tccctgtagc cggagggtta ttttccaagg gttgagtcgc
14881 gggacccccg gttcgagtct cgggccggcc ggactgcggc gaacgggggt ttgcctcccc
14941 gtcatgcaag accccgcttg caaattcctc cggaaacagg gacgagcccc ttttttgctt
15001 ttcccagatg catccggtgc tgcggcagat gcgcccccct cctcagcagc ggcaagagca
15061 agagcagcgg cagacatgca gggcaccctc cccttctcct accgcgtcag gaggggcaac
15121 atccgcggct gacgcggcgg cagatggtga ttacgaaccc ccgcggcgcc ggacccggca
15181 ctacttggac ttggaggagg gcgagggcct ggcgcggcta ggagcgccct ctcctgagcg
15241 acacccaagg gtgcagctga agcgtgacac gcgcgaggcg tacgtgccgc ggcagaacct
15301 gtttcgcgac cgcgagggag aggagcccga ggagatgcgg gatcgaaagt tccatgcagg
15361 gcgcgagttg cggcatggcc tgaaccgcga gcggttgctg cgcgaggagg actttgagcc
15421 cgacgcgcgg accgggatta gtcccgcgcg cgcacacgtg gcggccgccg acctggtaac
15481 cgcgtacgag cagacggtga accaggagat taactttcaa aaaagcttta acaaccacgt
15541 gcgcacgctt gtggcgcgcg aggaggtggc tataggactg atgcatctgt gggactttgt
15601 aagcgcgctg gagcaaaacc caaatagcaa gccgctcatg gcgcagctgt tccttatagt
15661 gcagcacagc agggacaacg aggcattcag ggatgcgctg ctaaacatag tagagcccga
15721 gggccgctgg ctgctcgatt tgataaacat tctgcagagc atagtggtgc aggagcgcag
15781 cttgagcctg gctgacaagg tggccgccat taactattcc atgctcagtc tgggcaagtt
15841 ttacgcccgc aagatatacc atacccctta cgttcccata gacaaggagg taaagatcga
15901 ggggttctac atgcgcatgg cgctgaaggt gcttaccttg agcgacgacc tgggcgttta
15961 tcgcaacgag cgcatccaca aggccgtgag cgtgagccgg cggcgcgagc tcagcgaccg
16021 cgagctgatg cacagcctgc aaagggccct ggctggcacg ggcagcggcg atagagaggc
16081 cgagtcctac tttgacgcgg gcgctgacct gcgctgggcc ccaagccgac gcgccctgga
16141 ggcagctggg gccggacctg ggctggcggt ggcacccgcg cgcgctggca acgtcggcgg
16201 cgtggaggaa tatgacgagg acgatgagta cgagccagag gacggcgagt actaagcggt
16261 gatgtttctg atcagatgat gcaagacgca acggacccgg cggtgcgggc ggcgctgcag
16321 agccagccgt ccggccttaa ctccacggac gactggcgcc aggtcatgga ccgcatcatg
16381 tcgctgactg cgcgcaaccc tgacgcgttc cggcagcagc cgcaggccaa ccggctctcc
16441 gcaattctgg aagcggtggt cccggcgcgc gcaaacccca cgcacgagaa ggtgctggcg
16501 atcgtaaacg cgctggccga aaacagggcc atccggcccg atgaggccgg cctggtctac

FIG. 4F

```
16561 gacgcgctgc ttcagcgcgt ggctcgttac aacagcagca acgtgcagac caacctggac
16621 cggctggtgg gggatgtgcg cgaggccgtg gcgcagcgtg agcgcgcgca gcagcagggc
16681 aacctgggct ccatggttgc actaaacgcc ttcctgagta cacagcccgc caacgtgccg
16741 cggggacagg aggactacac caactttgtg agcgcactgc ggctaatggt gactgagaca
16801 ccgcaaagtg aggtgtatca gtccgggcca gactattttt tccagaccag tagacaaggc
16861 ctgcagaccg taaacctgag ccaggctttc aagaacttgc aggggctgtg gggggtgcgg
16921 gctcccacag gcgaccgcgc gaccgtgtct agcttgctga cgcccaactc gcgcctgttg
16981 ctgctgctaa tagcgccctt cacggacagt ggcagcgtgt cccgggacac atacctaggt
17041 cacttgctga cactgtaccg cgaggccata ggtcaggcgc atgtggacga gcatactttc
17101 caggagatta caagtgttag ccgcgcgctg gggcaggagg acacgggcag cctggaggca
17161 accctgaact acctgctgac caaccggcgg caaaaaatcc cctcgttgca cagtttaaac
17221 agcgaggagg agcgcatttt gcgctatgtg cagcagagcg tgagccttaa cctgatgcgc
17281 gacggggtaa cgcccagcgt ggcgctggac atgaccgcgc gcaacatgga accgggcatg
17341 tatgcctcaa accggccgtt tatcaatcgc ctaatggact acttgcatcg cgcggccgcc
17401 gtgaaccccg agtatttcac caatgccatc ttgaacccgc actggctacc gccccctggt
17461 ttctacaccg ggggattcga ggtgcccgag ggtaacgatg gattcctctg ggacgacata
17521 gacgacagcg tgttttcccc gcaaccgcag accctgctag agttgcaaca acgcgagcag
17581 gcagaggcgg cgctgcgaaa ggaaagcttc cgcaggccaa gcagcttgtc cgatctaggc
17641 gctgcggccc cgcggtcaga tgctagtagc ccatttccaa gcttgatagg gtctcttacc
17701 agcactcgca ccacccgccc gcgcctgctg ggcgaggagg agtacctaaa caactcgctg
17761 ctgcagccgc agcgcgaaaa gaacctgcct ccggcgtttc ccaacaacgg gatagagagc
17821 ctagtggaca agatgagtag atggaagacg tatgcgcagg agcacaggga tgtgcccggc
17881 ccgcgcccgc ccacccgtcg tcaaaggcac gaccgtcagc ggggtctggt gtgggaggac
17941 gatgactcgg cagacgacag cagcgtcttg gatttgggag ggagtggcaa cccgtttgca
18001 caccttcgcc ccaggctggg gagaatgttt taaaaaaaag catgatgcaa aataaaaaac
18061 tcaccaaggc catggcaccg agcgttggtt ttcttgtatt ccccttagta tgcggcgcgc
18121 ggcgatgtat gaggaaggtc ctcctccctc ctacgagagc gtggtgagcg cggcgccagt
18181 ggcggcggcg ctgggttcac ccttcgatgc tcccctggac ccgccgttcg tgcctccgcg
18241 gtacctgcgg cctaccgggg ggagaaacag catccgttac tctgagttgg cacccctatt
18301 cgacaccacc cgtgtgtacc ttgtggacaa caagtcaacg gatgtggcat ccctgaacta
18361 ccagaacgac cacagcaact ttctaaccac ggtcattcaa aacaatgact acagcccggg
18421 ggaggcaagc acacagacca tcaatcttga cgaccggtcg cactggggcg gcgacctgaa
18481 aaccatcctg cataccaaca tgccaaatgt gaacgagttc atgtttacca ataagtttaa
18541 ggcgcgggtg atggtgtcgc gctcgcttac taaggacaaa caggtggagc tgaaatacga
18601 gtgggtggag ttcacgctgc ccgagggcaa ctactccgag accatgacca tagaccttat
18661 gaacaacgcg atcgtggagc actacttgaa agtgggcagg cagaacgggg ttctggaaag
18721 cgacatcggg gtaaagtttg acacccgcaa cttcagactg gggtttgacc cagtcactgg
18781 tcttgtcatg cctggggtat atacaaacga agccttccat ccagacatca ttttgctgcc
18841 aggatgcggg gtggacttca cccacagccg cctgagcaac ttgttgggca tccgcaagcg
18901 gcaacccttc caggagggct ttaggatcac ctacgatgac ctggagggtg gtaacattcc
18961 cgcactgttg gatgtggacg cctaccaggc aagcttgaaa gatgacaccg aacagggcgg
19021 gggtggcgca ggcggcggca acaacagtgg cagcggcgcg gaagagaact ccaacgcggc
19081 agctgcggca atgcagccgg tggaggacat gaacgatcat gccattcgcg gcgacacctt
19141 tgccacacgg gcggaggaga agcgcgctga ggccgaggca gcggccgaag ctgccgcccc
19201 cgctgcggag gctgcacaac ccgaggtcga gaagcctcag aagaaaccgg tgattaaacc
19261 cctgacagag gacagcaaga aacgcagtta caacctaata agcaatgaca gcaccttcac
19321 ccagtaccgc agctggtacc ttgcatacaa ctacggcgac cctcaggccg ggatccgctc
19381 atggaccctg ctttgcactc ctgacgtaac ctgcggctcg gagcaggtat actggtcgtt
19441 gcccgacatg atgcaagacc ccgtgacctt ccgctccacg cgccagatca gcaactttcc
19501 ggtggtgggc gccgagctgt tgcccgtgca ctccaagagc ttctacaacg accaggccgt
19561 ctactcccag ctcatccgcc agtttacctc tctgacccac gtgttcaatc gctttcccga
19621 gaaccagatt ttggcgcgcc cgccagcccc caccatcacc accgtcagtg aaaacgttcc
19681 tgctctcaca gatcacggga cgctaccgct gcgcaacagc atcggaggag tccagcgagt
19741 gaccattact gacgccagac gccgcacctg cccctacgtt tacaaggccc tgggcatagt
19801 ctcgccgcgc gtcctatcga gccgcacttt ttgagcaagc atgtccatcc ttatatcgcc
```

FIG. 4G

19861 cagcaataac acaggctggg gcctgcgctt cccaagcaag atgtttggcg gggccaagaa
19921 gcgctccgac caacacccag tgcgcgtgcg cgggcactac cgcgcgccct ggggcgcgca
19981 caaacgcggc cgcactgggc gcaccaccgt cgatgacgcc atcgacgcgg tggtggagga
20041 ggcgcgcaac tacacgccca cgccgccgcc agtgtccacc gtggacgcgg ccattcagac
20101 cgtggtgcgc ggagcccggc gctacgctaa aatgaagaga cggcggaggc gcgtagcacg
20161 tcgccaccgc cgccgacccg gcactgccgc ccaacgcgcg gcggcggccc tgcttaaccg
20221 cgcacgtcgc accggccgac gggcggccat gcgagccgct cgaaggctgg ccgcgggtat
20281 tgtcactgtg ccccccaggt ccaggcgacg agcggccgcc gcagcagccg cggccattag
20341 tgctatgact cagggtcgca ggggcaacgt gtactgggtg cgcgactcgg ttagcggcct
20401 gcgcgtgccc gtgcgcaccc gcccccgcg caactagatt gcaataaaaa actacttaga
20461 ctcgtactgt tgtatgtatc cagcggcggc ggcgcgcatc gaagctatgt ccaagcgcaa
20521 aatcaaagaa gagatgctcc aggtcatcgc gccggagatc tatggccccc cgaagaagga
20581 agagcaggat tacaagcccc gaaagctaaa gcgggtcaaa aagaaaaaga aagatgatga
20641 tgatgatgaa cttgacgacg aggtggaact gttgcacgcg accgcgccca ggcgacgggt
20701 acagtggaaa ggtcgacgcg taagacgtgt tttgcgaccc ggcaccaccg tagtctttac
20761 gcccggtgag cgctccaccc gcacctacaa gcgcgtgtat gatgaggtgt acggcgacga
20821 ggacctgctt gagcaggcca acgagcgcct cggggagttt gcctacggaa agcggcataa
20881 ggacatgctg gcgttgccgc tggacgaggg caacccaaca cctagcctaa agcccgtgac
20941 actgcagcag gtgctgcccg cgcttgcacc gtccgaagaa aagcgcggcc taaagcgcga
21001 gtctggtgac ttggcaccca ccgtgcagct gatggtaccc aagcgtcagc gactggaaga
21061 tgtcttggaa aaaatgaccg tggagcctgg gctggagccc gaggtccgcg tgcggccaat
21121 caagcaggtg gcaccgggac tgggcgtgca gaccgtggac gttcagatac ccaccaccag
21181 tagcactagt attgccactg ccacagaggg catggagaca caaacgtccc cggttgcctc
21241 ggcggtggca gatgccgcgg tgcaggcggc cgctgcggcc gcgtccaaga cctctacgga
21301 ggtgcaaacg gacccgtgga tgtttcgtgt ttcagccccc cggcgtccgc gccgttcaag
21361 gaagtacggc gccgccagcg cgctactgcc cgaatatgcc ctacatcctt ccatcgcgcc
21421 tacccccggc tatcgtggct acacctaccg ccccagaaga cgagcaacta cccgacgccg
21481 aaccaccact ggaacccgcc gccgccgtcg ccgtcgccag cccgtgctgg ccccgatttc
21541 cgtgcgcagg gtggctcgcg aaggaggcag gaccctggtg ctgccaacag cgcgctacca
21601 ccccagcatc gtttaaaagc cggtctttgt ggttcttgca gatatggccc tcacctgccg
21661 cctccgtttc ccggtgccgg gattccgagg aagaatgcac cgtaggaggg gcatggccgg
21721 ccacggcctg acgggcggca tgcgtcgtgc gcaccaccgg cggcggcgcg cgtcgcaccg
21781 tcgcatgcgc ggcggtatcc tgcccctcct tattccactg atcgccgcgg cgattggcgc
21841 cgtgcccgga attgcatccg tggccttgca ggcgcagaga cactgattaa aaacaagtta
21901 catgtggaaa aatcaaaata aaagtctgga ctctcacgct cgcttggtcc tgtaactatt
21961 ttgtagaatg gaagacatca actttgcgtc actggccccg cgacacggct cgcgcccgtt
22021 catgggaaac tggcaagata tcggcaccag caatatgagc ggtggcgcct tcagctgggg
22081 ctcgctgtgg agcggcatta aaaatttcgg ttccgccgtt aagaactatg gcagcaaagc
22141 ctggaacagc agcacaggcc agatgctgag ggacaagttg aaagagcaaa atttccaaca
22201 aaaggtggta gatggcctgg cctctggcat tagcggggtg gtggacctgg ccaaccaggc
22261 agtgcaaaat aagattaaca gtaagcttga tccccgccct cccgtagagg agcctccacc
22321 ggccgtggag acagtgtctc cagaggggcg tggcgaaaag cgtccgcgac ccgacaggga
22381 agaaactctg gtgacgcaaa tagacgagcc tccctcgtac gaggaggcac taaagcaagg
22441 cctgcccacc acccgtccca tcgcgcccat ggctaccgga gtgctgggcc agcacacacc
22501 cgtaacgctg gacctgcctc cccccgccga cacccagcag aaacctgtgc tgccaggccc
22561 gtccgccgtt gttgtaaccc gtcctagccg cgcgtccctg cgccgcgccg ccagcggtcc
22621 gcgatcgttg cggcccgtag ccagtggcaa ctggcaaagc acactgaaca gcatcgtggg
22681 tttgggggtg caatccctga agcgccgacg atgcttctga tagctaacgt gtcgtatgtg
22741 tgtcatgtat gcgtccatgt cgccgccaga ggagctgctg agccgccgcg cgcccgcttt
22801 ccaagatggc taccccttcg atgatgccgc agtggtctta catgcacatc tcgggccagg
22861 acgcctcgga gtacctgagc cccgggctgg tgcagttcgc ccgcgccacc gagacgtact
22921 tcagcctgaa taacaagttt agaaacccca cggtggcgcc tacgcacgac gtgaccacag
22981 accggtctca gcgtttgacg ctgcggttca tccccgtgga ccgcgaggat actgcgtact
23041 cgtacaaggc gcggttcacc ctagctgtgg gtgataaccg tgtgctagac atggcttcca
23101 cgtactttga catccgcggc gtgctggaca ggggccctac ttttaagccc tactctggca

FIG. 4H

23161 ctgcctacaa cgcactggcc cccaagggtg cccccaactc gtgcgagtgg gaacaaaatg
23221 aaactgcaca agtggatgct caagaacttg acgaagagga gaatgaagcc aatgaagctc
23281 aggcgcgaga acaggaacaa gctaagaaaa cccatgtata tgcccaggct ccactgtccg
23341 gaataaaaat aactaaagaa ggtctacaaa taggaactgc cgacgccaca gtagcaggtg
23401 ccggcaaaga aattttcgca gacaaaactt ttcaacctga accacaagta ggagaatctc
23461 aatggaacga agcggatgcc acagcagctg gtggaagggt tcttaaaaag acaactccca
23521 tgaaaccctg ctatggctca tacgctagac ccaccaattc caacggcgga cagggcgtta
23581 tggttgaaca aaatggtaaa ttggaaagtc aagtcgaaat gcaatttttt tccacatcca
23641 caaatgccac aaatgaagtt aacaatatac aaccaacagt tgtattgtac agcgaagatg
23701 taaacatgga aactccagat actcatcttt cttataaacc taaaatgggg gataaaaatg
23761 ccaaagtcat gcttggacaa caagcaatgc caaacagacc aaattacatt gcttttagag
23821 acaattttat tggtctcatg tattacaaca gcacaggtaa catgggtgtc cttgctggtc
23881 aggcatcgca gttgaacgct gttgtagatt tgcaagacag aaacacagag ctgtcctacc
23941 agcttttgct tgattcaatt ggcgacagaa caagatactt ttcaatgtgg aatcaagctg
24001 ttgacagcta tgatccagat gtcagaatta ttgagaacca tggaactgag gatgagttgc
24061 caaattattg ctttcctctt ggtggaattg ggattactga cacttttcaa gctgttaaaa
24121 caactgctgc taacggggac caaggcaata ctacctggca aaaagattca acatttgcag
24181 aacgcaatga aataggggtg ggaaataact ttgccatgga aattaacctg aatgccaacc
24241 tatggagaaa tttcctttac tccaatattg cgctgtacct gccagacaag ctaaaataca
24301 accccaccaa tgtggaaata tctgacaacc ccaacaccta cgactacatg aacaagcgag
24361 tggtggctcc tgggcttgta gactgctaca ttaaccttgg ggcgcgctgg tctctggact
24421 acatggacaa cgttaatccc tttaaccacc accgcaatgc gggcctgcgt taccgctcca
24481 tgttgttggg aaacggccgc tacgtgccct ttcacattca ggtgccccaa aagttttttg
24541 ccattaaaaa cctcctcctc ctgccaggct catacacata tgaatggaac ttcaggaagg
24601 atgttaacat ggttctgcag agctctctgg gaaacgacct tagagttgac ggggctagca
24661 ttaagtttga cagcatttgt ctttacgcca ccttcttccc catggcccac aacacggcct
24721 ccacgctgga agccatgctc agaaatgaca ccaacgacca gtcctttaat gactaccttt
24781 ccgccgccaa catgctatat cccatacccg ccaacgccac caacgtgccc atctccatcc
24841 catcgcgcaa ctgggcagca tttcgcggtt gggccttcac acgcttgaag acaaaggaaa
24901 ccccttccct gggatcaggc tacgaccctt actacaccta ctctggctcc ataccatacc
24961 ttgacggaac cttctatctt aatcacacct ttaagaaggt ggccattact tttgactctt
25021 ctgttagctg gccgggcaac gaccgcctgc ttactcccaa tgagtttgag attaagcgct
25081 cagttgacgg ggagggctat aacgtagctc agtgcaacat gacaaaggac tggttcctag
25141 tgcagatgtt ggccaactac aatattggct accagggctt ctacattcca gaaagctaca
25201 aagaccgcat gtactcgttc ttcagaaact tccagcccat gagccggcaa gtggtggacg
25261 atactaaata caaagattat cagcaggttg gaattatcca ccagcataac aactcaggct
25321 tcgtaggcta cctcgctccc accatgcgcg agggacaagc ttaccccgct aatgttccct
25381 acccactaat aggcaaaacc gcggttgata gtattaccca gaaaaagttt ctttgcgacc
25441 gcaccctgtg gcgcatcccc ttctccagta actttatgtc catgggtgcg ctcacagacc
25501 tgggccaaaa ccttctctac gcaaactccg cccacgcgct agacatgacc tttgaggtgg
25561 atcccatgga cgagcccacc cttctttatg ttttgtttga agtctttgac gtggtccgtg
25621 tgcaccagcc gcaccgcggc gtcatcgaga ccgtgtacct gcgcacgccc ttctcggccg
25681 gcaacgccac aacataaaga agcaagcaac atcaacaaca gctgccgcca tgggctccag
25741 tgagcaggaa ctgaaagcca ttgtcaaaga tcttggttgt gggccatatt ttttgggcac
25801 ctatgacaag cgcttcccag gctttgtttc cccacacaag ctcgcctgcg ccatagttaa
25861 cacggccggt cgcgagactg gggcgtaca ctggatggcc tttgcctgga acccgcgctc
25921 aaaaacatgc tacctctttg agccctttgg cttttctgac caacgtctca agcaggttta
25981 ccagtttgag tacgagtcac tcctgcgccg tagcgccatt gcctcttccc ccgaccgctg
26041 tataacgctg gaaaagtcca cccaaagcgt gcaggggccc aactcggccg cctgtggcct
26101 attctgctgc atgtttctcc acgcctttgc caactggccc caaactccca tggatcacaa
26161 ccccaccatg aaccttatta ccggggtacc caactccatg cttaacagtc cccaggtaca
26221 gcccaccctg cgccgcaacc aggaacagct ctacagcttc ctggagcgcc actcgcccta
26281 cttccgcagc cacagtgcgc aaattaggag cgccacttct ttttgtcact tgaaaaacat
26341 gtaaaaataa tgtactagga gacactttca ataaaggcaa atgtttttat ttgtacactc
26401 tcgggtgatt atttaccccc acccttgccg tctgcgccgt ttaaaaatca aaggggttct

FIG. 4I

26461 gccgcgcatc gctatgcgcc actggcaggg acacgttgcg atactggtgt ttagtgctcc
26521 acttaaactc aggcacaacc atccgcggca gctcggtgaa gttttcactc cacaggctgc
26581 gcaccatcac caacgcgttt agcaggtcgg gcgccgatat cttgaagtcg cagttggggc
26641 ctccgccctg cgcgcgcgag ttgcgataca cagggttaca gcactggaac actatcagcg
26701 ccgggtggtg cacgctggcc agcacgctct tgtcggagat cagatccgcg tccaggtcct
26761 ccgcgttgct cagggcgaac ggagtcaact ttggtagctg ccttcccaaa aagggtgcat
26821 gcccaggctt tgagttgcac tcgcaccgta gtggcatcag aaggtgaccg tgcccagtct
26881 gggcgttagg atacagcgcc tgcatgaaag ccttgatctg cttaaaagcc acctgagcct
26941 ttgcgccttc agagaagaac atgccgcaag acttgccgga aaactgattg gccggacagg
27001 ccgcgtcatg cacgcagcac cttgcgtcgg tgttggagat ctgcaccaca tttcggcccc
27061 accggttctt cacgatcttg gccttgctag actgctcctt cagcgcgcgc tgcccgtttt
27121 cgctcgtcac atccatttca atcacgtgct ccttatttat cataatgctc ccgtgtagac
27181 acttaagctc gccttcgatc tcagcgcagc ggtgcagcca caacgcgcag cccgtgggct
27241 cgtggtgctt gtaggttacc tctgcaaacg actgcaggta cgcctgcagg aatcgcccca
27301 tcatcgtcac aaaggtcttg ttgctggtga aggtcagctg caacccgcgg tgctcctcgt
27361 ttagccaggt cttgcatacg gccgccagag cttccacttg gtcaggcagt agcttgaagt
27421 ttgcctttag atcgttatcc acgtggtact tgtccatcaa cgcgcgcgca gcctccatgc
27481 ccttctccca cgcagacacg atcggcaggc tcagcgggtt tatcaccgtg ctttcacttt
27541 ccgcttcact ggactcttcc ttttcctctt gcatccgcat accccgcgcc actgggtcgt
27601 cttcattcag ccgccgcacc gtgcgcttac ctcccttgcc gtgcttgatt agcaccggtg
27661 ggttgctgaa acccaccatt tgtagcgcca catcttctct ttcttcctcg ctgtccacga
27721 tcacctctgg ggatggcggg cgctcgggct tgggagaggg gcgcttcttt ttcttttttgg
27781 acgcaatggc caaatccgcc gtcgaggtcg atggccgcgg gctgggtgtg cgcggcacca
27841 gcgcatcttg tgacgagtct tcttcgtcct cggactcgag acgccgcctc agccgctttt
27901 ttgggggcgc gcggggaggc ggcggcgacg gcgacgggga cgagacgtcc tccatggttg
27961 gtggacgtcg cgccgcaccg cgtccgcgct cgggggtggt ttcgcgctgc tcctcttccc
28021 gactggccat ttccttctcc tataggcaga aaaagatcat ggagtcagtc gagaaggagg
28081 acagcctaac cgcccccttt gagttcgcca ccaccgcctc caccgatgcc gccaacgcgc
28141 ctaccacctt ccccgtcgag gcacccccgc ttgaggagga ggaagtgatt atcgagcagg
28201 acccaggttt tgtaagcgaa gacgacgaag atcgctcagt accaacagag gataaaaagc
28261 aagaccagga cgacgcagag gcaaacgagg aacaagtcgg gcggggggac caaaggcatg
28321 gcgactacct agatgtggga gacgacgtgc tgttgaagca tctgcagcgc cagtgcgcca
28381 ttatctgcga cgcgttgcaa gagcgcagcg atgtgcccct cgccatagcg gatgtcagcc
28441 ttgcctacga acgccacctg ttctcaccgc gcgtaccccc caaacgccaa gaaaacggca
28501 catgcgagcc caacccgcgc ctcaacttct accccgtatt tgccgtgcca gaggtgcttg
28561 ccacctatca catctttttc caaaactgca agatacccct atcctgccgt gccaaccgca
28621 gccgagcgga caagcagctg gccttgcggc agggcgctgt catacctgat atcgcctcgc
28681 tcgacgaagt gccaaaaatc tttgagggtc ttggacgcga cgagaagcgc gcggcaaacg
28741 ctctgcaaca agaaaacagc gaaaatgaaa gtcactgtgg agtgctggtg gaacttgagg
28801 gtgacaacgc gcgcctagcc gtgctgaaac gcagcatcga ggtcacccac tttgcctacc
28861 cggcacttaa cctacccccc aaggttatga gcacagtcat gagcgagctg atcgtgcgcc
28921 gtgcacgacc cctggagagg gatgcaaact tgcaagaaca aaccgaggag ggcctacccg
28981 cagttggcga tgagcagctg gcgcgctggc ttgagacgcg cgagcctgcc gacttggagg
29041 agcgacgcaa gctaatgatg gccgcagtgc ttgttaccgt ggagcttgag tgcatgcagc
29101 ggttctttgc tgacccggag atgcagcgca agctagagga aacgttgcac tacacctttc
29161 gccagggcta cgtgcgccag gcctgcaaaa tttccaacgt ggagctctgc aacctggtct
29221 cctaccttgg aattttgcac gaaaaccgcc ttgggcaaaa cgtgcttcat tccacgctca
29281 agggcgaggc gcgccgcgac tacgtccgcg actgcgttta cttatttctg tgctacacct
29341 ggcaaacggc catgggcgtg tggcagcagt gcctggagga gcgcaacctg aaggagctgc
29401 agaagctgct aaagcaaaac ttgaaggacc tatggacggc cttcaacgag cgctccgtgg
29461 ccgcgcacct ggcggacatt atcttccccg aacgcctgct taaaaccctg caacagggtc
29521 tgccagactt caccagtcaa agcatgttgc aaaactttag gaactttatc ctagagcgtt
29581 caggaattct gcccgccacc tgctgtgcgc ttcctagcga ctttgtgccc attaagtacc
29641 gtgaatgccc tccgccgctt tggggtcact gctaccttct gcagctagcc aactaccttg
29701 cctaccactc cgacatcatg gaagacgtga gcggtgacgg cctactggag tgtcactgtc

FIG. 4J

```
29761 gctgcaacct atgcaccccg caccgctccc tggtctgcaa ttcacaactg cttagcgaaa
29821 gtcaaattat cggtaccttt gagctgcagg gtccctcgcc tgacgaaaag tccgcggctc
29881 cggggttgaa actcactccg ggctgtgga cgtcggctta ccttcgcaaa tttgtacctg
29941 aggactacca cgcccacgag attaggttct acgaagacca atcccgcccg ccaaatgcgg
30001 agcttaccgc ctgcgtcatt acccagggcc acatccttgg ccaattgcaa gccattaaca
30061 aagcccgcca agagtttctg ctacgaaagg gacgggggt ttacttggac ccccagtccg
30121 gcgaggagct caacccaatc cccccgccgc cgcagcccta tcagcagccg cgggcccttg
30181 cttcccagga tggcacccaa aaagaagctg cagctgccgc cgccgccacc cacggacgag
30241 gaggaatact gggacagtca ggcagaggag gttttggacg aggaggagga gatgatggaa
30301 gactgggaca gcctagacga ggaagcttcc gaggccgaag aggtgtcaga cgaaacaccg
30361 tcaccctcgg tcgcattccc ctcgccggcg ccccagaaat cggcaaccgt tcccagcatt
30421 gctacaacct ccgctcctca ggcgccgccg gcactgcccg ttcgccgacc caaccgtaga
30481 tgggacacca ctggaaccag ggccggtaag tctaagcagc cgccgccgtt agcccaagag
30541 caacaacagc gccaaggcta ccgctcgtgg cgcgtgcaca agaacgccat agttgcttgc
30601 ttgcaagact gtgggggcaa catctccttc gcccgccgct ttcttctcta ccatcacggc
30661 gtggccttcc cccgtaacat cctgcattac taccgtcatc tctacagccc ctactgcacc
30721 ggcggcagcg gcagcaacag cagcggccac gcagaagcaa aggcgaccgg atagcaagac
30781 tctgacaaag cccaagaaat ccacagcggc ggcagcagca ggaggaggag cactgcgtct
30841 ggcgcccaac gaacccgtat cgacccgcga gcttagaaac aggatttttc ccactctgta
30901 tgctatattt caacagagca ggggccaaga acaagagctg aaaataaaaa acaggtctct
30961 gcgctccctc acccgcagct gcctgtatca caaaagcgaa gatcagcttc ggcgcacgct
31021 ggaagacgcg gaggctctct tcagcaaata ctgcgcgctg actcttaagg actagtttcg
31081 cgccctttct caaatttaag cgcgaaaact acgtcatctc cagcggccac acccggcgcc
31141 agcacctgtc gtcagcgcca ttatgagcaa ggaaattccc acgccctaca tgtggagtta
31201 ccagccacaa atgggacttg cggctggagc tgcccaagac tactcaaccc gaataaacta
31261 catgagcgcg ggaccccaca tgatatcccg ggtcaacgga atccgcgccc accgaaaccg
31321 aattctcctc gaacaggcgg ctattaccac cacacctcgt aataacctta atccccgtag
31381 ttggcccgct gccctggtgt accaggaaag tcccgctccc accactgtgg tacttcccag
31441 agacgcccag gccgaagttc agatgactaa ctcaggggcg cagcttgcgg gcggctttcg
31501 tcacagggtg cggtcgcccg ggcagggtat aactcacctg aaaatcagag ggcgaggtat
31561 tcagctcaac gacgagtcgg tgagctcctc tcttggtctc cgtccggacg ggacatttca
31621 gatcggcggc gctggccgct cttcatttac gccccgtcag gcgatcctaa ctctgcagac
31681 ctcgtcctcg gagccgcgct ccggaggcat tggaactcta caatttattg aggagttcgt
31741 gccttcggtt tacttcaacc cctttctgg acctcccggc cactacccgg accagtttat
31801 tcccaacttt gacgcggtaa aagactcggc ggacggctac gactgaatga ccagtggaga
31861 ggcagagcaa ctgcgcctga cacacctcga ccactgccgc cgccacaagt gctttgcccg
31921 cggctccggt gagttttgtt actttgaatt gcccgaagag catatcgagg gcccggcgca
31981 cggcgtccgg ctcaccaccc aggtagagct tacacgtagc ctgattcggg agtttaccaa
32041 gcgccccctg ctagtggagc gggagcgggg tccctgtgtt ctgaccgtgg tttgcaactg
32101 tcctaaccct ggattacatc aagatcttat tccattcaac taacaataaa cacacaataa
32161 attacttact taaaatcagt cagcaaatct ttgtccagct tattcagcat cacctccttt
32221 ccctcctccc aactctggta tttcagcagc cttttagctg cgaactttct ccaaagtcta
32281 aatgggatgt caaattcctc atgttcttgt ccctccgcac ccactatctt catattgttg
32341 cagatgaaac gcgccagacc gtctgaagac accttcaacc ctgtgtaccc atatgacacg
32401 gaaaccggcc ctccaactgt gcctttcctt acccctccct ttgtgtcgcc aaatgggttc
32461 caagaaagtc cccccggagt gctttctttg cgtctttcag aacctttggt tacctcacac
32521 ggcatgcttg cgctaaaaat gggcagcggc ctgtccctgg atcaggcagg caaccttaca
32581 tcaaatacaa tcactgtttc tcaaccgcta aaaaaaacaa agtccaatat aactttggaa
32641 acatccgcgc cccttacagt cagctcaggc gccctaacca tggccacaac ttcgcctttg
32701 gtggtctctg acaacactct taccatgcaa tcacaagcac cgctaaccgt gcaagactca
32761 aaacttagca ttgctaccaa agagccactt acagtgttag atggaaaact ggccctgcag
32821 acatcagccc ccctctctgc cactgataac aacgccctca ctatcactgc ctcacctcct
32881 cttactactg caaatggtag tctggctgtt accatggaaa acccacttta caacaacaat
32941 ggaaaacttg ggctcaaaat tggcggtcct ttgcaagtgg ccaccgactc acatgcacta
33001 acactaggta ctggtcaggg ggttgcagtt cataacaatt tgctacatac aaaagttaca
```

FIG. 4K

33061 ggcgcaatag ggtttgatac atctggcaac atggaactta aaactggaga tggcctctat
33121 gtggatagcg ccggtcctaa ccaaaaacta catattaatc taaataccac aaaaggcctt
33181 gcttttgaca acaccgcaat aacaattaac gctggaaaag ggttggaatt tgaaacagac
33241 tcctcaaacg gaaatcccat aaaaacaaaa attggatcag gcatacaata taataccaat
33301 ggagctatgg ttgcaaaact tggaacaggc ctcagttttg acagctccgg agccataaca
33361 atgggcagca taaacaatga cagacttact ctttggacaa caccagaccc atccccaaat
33421 tgcagaattg cttcagataa agactgcaag ctaactctgg cgctaacaaa atgtggcagt
33481 caaattttgg gcactgtttc agctttggca gtatcaggta atatggcctc catcaatgga
33541 actctaagca gtgtaaactt ggttcttaga tttgatgaca acggagtgct tatgtcaaat
33601 tcatcactgg acaaacagta ttggaacttt agaaacgggg actccactaa cggtcaacca
33661 tacacttatg ctgttgggtt tatgccaaac ctaaaagctt acccaaaaac tcaaagtaaa
33721 actgcaaaaa gtaatattgt tagccaggtg tatcttaatg gtgacaagtc taaaccattg
33781 cattttacta ttacgctaaa tggaacagat gaaaccaacc aagtaagcaa atactcaata
33841 tcattcagtt ggtcctggaa cagtggacaa tacactaatg acaaatttgc caccaattcc
33901 tataccttct cctacattgc ccaggaataa agaatcgtga acctgttgca tgttatgttt
33961 caacgtgttt atttttcaat tgcagaaaat ttcaagtcat ttttcattca gtagtatagc
34021 cccaccacca catagcttat actaatcacc gtaccttaat caaactcaca gaaccctagt
34081 attcaacctg ccacctccct cccaacacac agagtacaca gtcctttctc cccggctggc
34141 cttaaacagc atcatatcat gggtaacaga catattctta ggtgttatat tccacacggt
34201 ctcctgtcga gccaaacgct catcagtgat gttaataaac tccccgggca gctcgcttaa
34261 gttcatgtcg ctgtccagct gctgagccac aggctgctgt ccaacttgcg gttgctcaac
34321 gggcggcgaa ggagaagtcc acgcctacat gggggtagag tcataatcgt gcatcaggat
34381 agggcggtgg tgctgcagca gcgcgcgaat aaactgctgc cgccgccgct ccgtcctgca
34441 ggaatacaac atggcagtgg tctcctcagc gatgattcgc accgcccgca gcataaggcg
34501 ccttgtcctc cgggcacagc agcgcaccct gatctcactt aagtcagcac agtaactgca
34561 gcacagtacc acaatattgt ttaaaatccc acagtgcaag gcgctgtatc caaagctcat
34621 ggcggggacc acagaaccca cgtggccatc ataccacaag cgcaggtaga ttaagtggcg
34681 acccctcata aacacgctgg acataaacat tacctctttt ggcatgttgt aattcaccac
34741 ctcccggtac catataaacc tctgattaaa catggcgcca tccaccacca tcctaaacca
34801 gctggccaaa acctgcccgc cggctatgca ctgcagggaa ccgggactgg aacaatgaca
34861 gtggagagcc caggactcgt aaccatggat catcatgctc gtcatgatat caatgttggc
34921 acaacacagg cacacgtgca tacacttcct caggattaca agctcctccc gcgtcagaac
34981 catatcccag ggaacaaccc attcctgaat cagcgtaaat cccacactgc agggaagacc
35041 tcgcacgtaa ctcacgttgt gcattgtcaa agtgttacat tcgggcagca gcggatgatc
35101 ctccagtatg gtagcgcggg tttctgtctc aaaaggaggt agacgatccc tactgtacgg
35161 agtgcgccga gacaaccgag atcgtgttgg tcgtagtgtc atgccaaatg gaacgccgga
35221 cgtagtcata tttcctgaag caaaaccagg tgcgggcgtg acaaacagat ctgcgtctcc
35281 ggtctcgccg cttagatcgc tctgtgtagt agttgtagta tatccactct ctcaaagcat
35341 ccaggcgccc cctggcttcg ggttctatgt aaactccttc atgcgccgct gccctgataa
35401 catccaccac cgcagaataa gccacaccca gccaacctac acattcgttc tgcgagtcac
35461 acacgggagg agcgggaaga gctggaagaa ccatgttttt ttttttattc caaaagatta
35521 tccaaaacct caaaatgaag atctattaag tgaacgcgct cccctccggt ggcgtggtca
35581 aactctacag ccaaagaaca gataatggca tttgtaagat gttgcacaat ggcttccaaa
35641 aggcaaacgg ccctcacgtc caagtggacg taaaggctaa acccttcagg gtgaatctcc
35701 tctataaaca ttccagcacc ttcaaccatg cccaaataat tctcatctcg ccaccttctc
35761 aatatatctc taagcaaatc ccgaatatta agtccggcca ttgtaaaaat ctgctccaga
35821 gcgccctcca ccttcagcct caagcagcga atcatgattg caaaaattca ggttcctcac
35881 agacctgtat aagattcaaa agcggaacat taacaaaaat accgcgatcc cgtaggtccc
35941 ttcgcagggc cagctgaaca taatcgtgca ggtctgcacg gaccagcgcg gccacttccc
36001 cgccaggaac catgacaaaa gaacccacac tgattatgac acgcatactc ggagctatgc
36061 taaccagcgt agccccgatg taagcttgtt gcatgggcgg cgatataaaa tgcaaggtgc
36121 tgctcaaaaa atcaggcaaa gcctcgcgca aaaaagaaag cacatcgtag tcatgctcat
36181 gcagataaag gcaggtaagc tccggaacca ccacagaaaa agacaccatt tttctctcaa
36241 acatgtctgc gggtttctgc ataaacacaa aataaaataa caaaaaaaca tttaaacatt
36301 agaagcctgt cttacaacag gaaaaacaac ccttataagc ataagacgga ctacggccat

FIG. 4L

```
36361 gccggcgtga ccgtaaaaaa actggtcacc gtgattaaaa agcaccaccg acagctcctc
36421 ggtcatgtcc ggagtcataa tgtaagactc ggtaaacaca tcaggttgat tcacatcggt
36481 cagtgctaaa aagcgaccga aatagcccgg gggaatacat acccgcaggc gtagagacaa
36541 cattacagcc cccataggag gtataacaaa attaatagga gagaaaaaca cataaacacc
36601 tgaaaaaccc tcctgcctag gcaaaatagc accctcccgc tccagaacaa catacagcgc
36661 ttccacagcg gcagccataa cagtcagcct taccagtaaa aaagaaaacc tattaaaaaa
36721 acaccactcg acacggcacc agctcaatca gtcacagtgt aaaaaagggc caagtgcaga
36781 gcgagtatat ataggactaa aaaatgacgt aacggttaaa gtccacaaaa aacacccaga
36841 aaaccgcacg cgaacctacg cccagaaacg aaagccaaaa aacccacaac ttcctcaaat
36901 cgtcacttcc gttttcccac gttacgtcac ttcccatttt aagaaaacta caattcccaa
36961 cacatacaag ttactccgcc ctaaaaccta cgtcacccgc cccgttccca cgcccccgcgc
37021 cacgtcacaa actccacccc ctcattatca tattggcttc aatccaaaat aaggtatatt
37081 attgatgatg
```

FIG. 4M

```
10                 30                 50
ATGGCGCCCATCACGGCCTACTCCCAACAGACGCGGGGCCTACTTGGTTGCATCATCACT
---------+---------+---------+---------+---------+---------+
MetAlaProIleThrAlaTyrSerGlnGlnThrArgGlyLeuLeuGlyCysIleIleThr
                           10                            20

       70                 90                 110
AGCCTTACAGGCCGGGACAAGAACCAGGTCGAGGGAGAGGTTCAGGTGGTTTCCACCGCA
---------+---------+---------+---------+---------+---------+
SerLeuThrGlyArgAspLysAsnGlnValGluGlyGluValGlnValValSerThrAla
                           30                            40

       130                150                170
ACACAATCCTTCCTGGCGACCTGCGTCAACGGCGTGTGTTGGACCGTTTACCATGGTGCT
---------+---------+---------+---------+---------+---------+
ThrGlnSerPheLeuAlaThrCysValAsnGlyValCysTrpThrValTyrHisGlyAla
                           50                            60

       190                210                230
GGCTCAAAGACCTTAGCCGGCCCAAAGGGGCCAATCACCCAGATGTACACTAATGTGGAC
---------+---------+---------+---------+---------+---------+
GlySerLysThrLeuAlaGlyProLysGlyProIleThrGlnMetTyrThrAsnValAsp
                           70                            80

       250                270                290
CAGGACCTCGTCGGCTGGCAGGCGCCCCCCGGGGCGCGTTCCTTGACACCATGCACCTGT
---------+---------+---------+---------+---------+---------+
GlnAspLeuValGlyTrpGlnAlaProProGlyAlaArgSerLeuThrProCysThrCys
                           90                           100

       310                330                350
GGCAGCTCAGACCTTTACTTGGTCACGAGACATGCTGACGTCATTCCGGTGCGCCGGCGG
---------+---------+---------+---------+---------+---------+
GlySerSerAspLeuTyrLeuValThrArgHisAlaAspValIleProValArgArgArg
                          110                           120

       370                390                410
GGCGACAGTAGGGGGAGCCTGCTCTCCCCCAGGCCTGTCTCCTACTTGAAGGGCTCTTCG
---------+---------+---------+---------+---------+---------+
GlyAspSerArgGlySerLeuLeuSerProArgProValSerTyrLeuLysGlySerSer
                          130                           140
```

FIG. 5A

```
        430                 450                 470
GGTGGTCCACTGCTCTGCCCTTCGGGGCACGCTGTGGGCATCTTCCGGGCTGCCGTATGC
---------+---------+---------+---------+---------+---------+
GlyGlyProLeuLeuCysProSerGlyHisAlaValGlyIlePheArgAlaAlaValCys
                            150                           160

        490                 510                 530
ACCCGGGGGGTTGCGAAGGCGGTGGACTTTGTGCCCGTAGAGTCCATGGAAACTACTATG
---------+---------+---------+---------+---------+---------+
ThrArgGlyValAlaLysAlaValAspPheValProValGluSerMetGluThrThrMet
                            170                           180

        550                 570                 590
CGGTCTCCGGTCTTCACGGACAACTCATCCCCCCCGGCCGTACCGCAGTCATTTCAAGTG
---------+---------+---------+---------+---------+---------+
ArgSerProValPheThrAspAsnSerSerProProAlaValProGlnSerPheGlnVal
                            190                           200

        610                 630                 650
GCCCACCTACACGCTCCCACTGGCAGCGGCAAGAGTACTAAAGTGCCGGCTGCATATGCA
---------+---------+---------+---------+---------+---------+
AlaHisLeuHisAlaProThrGlySerGlyLysSerThrLysValProAlaAlaTyrAla
                            210                           220

        670                 690                 710
GCCCAAGGGTACAAGGTGCTCGTCCTCAATCCGTCCGTTGCCGCTACCTTAGGGTTTGGG
---------+---------+---------+---------+---------+---------+
AlaGlnGlyTyrLysValLeuValLeuAsnProSerValAlaAlaThrLeuGlyPheGly
                            230                           240

        730                 750                 770
GCGTATATGTCTAAGGCACACGGTATTGACCCCAACATCAGAACTGGGGTAAGGACCATT
---------+---------+---------+---------+---------+---------+
AlaTyrMetSerLysAlaHisGlyIleAspProAsnIleArgThrGlyValArgThrIle
                            250                           260

        790                 810                 830
ACCACAGGCGCCCCCGTCACATACTCTACCTATGGCAAGTTTCTTGCCGATGGTGGTTGC
---------+---------+---------+---------+---------+---------+
ThrThrGlyAlaProValThrTyrSerThrTyrGlyLysPheLeuAlaAspGlyGlyCys
                            270                           280
```

FIG. 5B

```
       850                 870                 890
TCTGGGGGCGCTTATGACATCATAATATGTGATGAGTGCCATTCAACTGACTCGACTACA
---------+---------+---------+---------+---------+---------+
SerGlyGlyAlaTyrAspIleIleIleCysAspGluCysHisSerThrAspSerThrThr
                              290                           300

       910                 930                 950
ATCTTGGGCATCGGCACAGTCCTGGACCAAGCGGAGACGGCTGGAGCGCGGCTTGTCGTG
---------+---------+---------+---------+---------+---------+
IleLeuGlyIleGlyThrValLeuAspGlnAlaGluThrAlaGlyAlaArgLeuValVal
                              310                           320

       970                 990                1010
CTCGCCACCGCTACGCCTCCGGGATCGGTCACCGTGCCACACCCAAACATCGAGGAGGTG
---------+---------+---------+---------+---------+---------+
LeuAlaThrAlaThrProProGlySerValThrValProHisProAsnIleGluGluVal
                              330                           340

      1030                1050                1070
GCCCTGTCTAATACTGGAGAGATCCCCTTCTATGGCAAAGCCATCCCCATTGAAGCCATC
---------+---------+---------+---------+---------+---------+
AlaLeuSerAsnThrGlyGluIleProPheTyrGlyLysAlaIleProIleGluAlaIle
                              350                           360

      1090                1110                1130
AGGGGGGGAAGGCATCTCATTTTCTGTCATTCCAAGAAGAAGTGCGACGAGCTCGCCGCA
---------+---------+---------+---------+---------+---------+
ArgGlyGlyArgHisLeuIlePheCysHisSerLysLysLysCysAspGluLeuAlaAla
                              370                           380

      1150                1170                1190
AAGCTGTCAGGCCTCGGAATCAACGCTGTGGCGTATTACCGGGGGCTCGATGTGTCCGTC
---------+---------+---------+---------+---------+---------+
LysLeuSerGlyLeuGlyIleAsnAlaValAlaTyrTyrArgGlyLeuAspValSerVal
                              390                           400

      1210                1230                1250
ATACCAACTATCGGAGACGTCGTTGTCGTGGCAACAGACGCTCTGATGACGGGCTATACG
---------+---------+---------+---------+---------+---------+
IleProThrIleGlyAspValValValValAlaThrAspAlaLeuMetThrGlyTyrThr
                              410                           420
```

FIG. 5C

```
        1270                1290                1310
GGCGACTTTGACTCAGTGATCGACTGTAACACATGTGTCACCCAGACAGTCGACTTCAGC
---------+---------+---------+---------+---------+---------+
GlyAspPheAspSerValIleAspCysAsnThrCysValThrGlnThrValAspPheSer
                              430                           440

        1330                1350                1370
TTGGATCCCACCTTCACCATTGAGACGACGACCGTGCCTCAAGACGCAGTGTCGCGCTCG
---------+---------+---------+---------+---------+---------+
LeuAspProThrPheThrIleGluThrThrThrValProGlnAspAlaValSerArgSer
                              450                           460

        1390                1410                1430
CAGCGGCGGGGTAGGACTGGCAGGGGTAGGAGAGGCATCTACAGGTTTGTGACTCCGGGA
---------+---------+---------+---------+---------+---------+
GlnArgArgGlyArgThrGlyArgGlyArgArgGlyIleTyrArgPheValThrProGly
                              470                           480

        1450                1470                1490
GAACGGCCCTCGGGCATGTTCGATTCCTCGGTCCTGTGTGAGTGCTATGACGCGGGCTGT
---------+---------+---------+---------+---------+---------+
GluArgProSerGlyMetPheAspSerSerValLeuCysGluCysTyrAspAlaGlyCys
                              490                           500

        1510                1530                1550
GCTTGGTACGAGCTCACCCCCGCCGAGACCTCGGTTAGGTTGCGGGCCTACCTGAACACA
---------+---------+---------+---------+---------+---------+
AlaTrpTyrGluLeuThrProAlaGluThrSerValArgLeuArgAlaTyrLeuAsnThr
                              510                           520

        1570                1590                1610
CCAGGGTTGCCCGTTTGCCAGGACCACCTGGAGTTCTGGGAGAGTGTCTTCACAGGCCTC
---------+---------+---------+---------+---------+---------+
ProGlyLeuProValCysGlnAspHisLeuGluPheTrpGluSerValPheThrGlyLeu
                              530                           540

        1630                1650                1670
ACCCACATAGATGCACACTTCTTGTCCCAGACCAAGCAGGCAGGAGACAACTTCCCCTAC
---------+---------+---------+---------+---------+---------+
ThrHisIleAspAlaHisPheLeuSerGlnThrLysGlnAlaGlyAspAsnPheProTyr
                              550                           560
```

FIG. 5D

```
        1690                1710                1730
CTGGTAGCATACCAAGCCACGGTGTGCGCCAGGGCTCAGGCCCCACCTCCATCATGGGAT
---------+---------+---------+---------+---------+---------+
LeuValAlaTyrGlnAlaThrValCysAlaArgAlaGlnAlaProProProSerTrpAsp
                              570                           580

        1750                1770                1790
CAAATGTGGAAGTGTCTCATACGGCTGAAACCTACGCTGCACGGGCCAACACCCTTGCTG
---------+---------+---------+---------+---------+---------+
GlnMetTrpLysCysLeuIleArgLeuLysProThrLeuHisGlyProThrProLeuLeu
                              590                           600

        1810                1830                1850
TACAGGCTGGGAGCCGTCCAAAATGAGGTCACCCTCACCCACCCCATAACCAAATACATC
---------+---------+---------+---------+---------+---------+
TyrArgLeuGlyAlaValGlnAsnGluValThrLeuThrHisProIleThrLysTyrIle
                              610                           620

        1870                1890                1910
ATGGCATGCATGTCGGCTGACCTGGAGGTCGTCACTAGCACCTGGGTGCTGGTGGGCGGA
---------+---------+---------+---------+---------+---------+
MetAlaCysMetSerAlaAspLeuGluValValThrSerThrTrpValLeuValGlyGly
                              630                           640

        1930                1950                1970
GTCCTTGCAGCTCTGGCCGCGTATTGCCTGACAACAGGCAGTGTGGTCATTGTGGGTAGG
---------+---------+---------+---------+---------+---------+
ValLeuAlaAlaLeuAlaAlaTyrCysLeuThrThrGlySerValValIleValGlyArg
                              650                           660

        1990                2010                2030
ATTATCTTGTCCGGGAGGCCGGCTATTGTTCCCGACAGGGAGTTTCTCTACCAGGAGTTC
---------+---------+---------+---------+---------+---------+
IleIleLeuSerGlyArgProAlaIleValProAspArgGluPheLeuTyrGlnGluPhe
                              670                           680

        2050                2070                2090
GATGAAATGGAAGAGTGCGCCTCGCACCTCCCTTACATCGAGCAGGGAATGCAGCTCGCC
---------+---------+---------+---------+---------+---------+
AspGluMetGluGluCysAlaSerHisLeuProTyrIleGluGlnGlyMetGlnLeuAla
                              690                           700
```

FIG. 5E

```
       2110                2130                2150
GAGCAATTCAAGCAGAAAGCGCTCGGGTTACTGCAAACAGCCACCAAACAAGCGGAGGCT
---------+---------+---------+---------+---------+---------+
GluGlnPheLysGlnLysAlaLeuGlyLeuLeuGlnThrAlaThrLysGlnAlaGluAla
                              710                         720

       2170                2190                2210
GCTGCTCCCGTGGTGGAGTCCAAGTGGCGAGCCCTTGAGACATTCTGGGCGAAGCACATG
---------+---------+---------+---------+---------+---------+
AlaAlaProValValGluSerLysTrpArgAlaLeuGluThrPheTrpAlaLysHisMet
                              730                         740

       2230                2250                2270
TGGAATTTCATCAGCGGGATACAGTACTTAGCAGGCTTATCCACTCTGCCTGGGAACCCC
---------+---------+---------+---------+---------+---------+
TrpAsnPheIleSerGlyIleGlnTyrLeuAlaGlyLeuSerThrLeuProGlyAsnPro
                              750                         760

       2290                2310                2330
GCAATAGCATCATTGATGGCATTCACAGCCTCTATCACCAGCCCGCTCACCACCCAAAGT
---------+---------+---------+---------+---------+---------+
AlaIleAlaSerLeuMetAlaPheThrAlaSerIleThrSerProLeuThrThrGlnSer
                              770                         780

       2350                2370                2390
ACCCTCCTGTTTAACATCTTGGGGGGTGGGTGGCTGCCCAACTCGCCCCCCCCAGCGCC
---------+---------+---------+---------+---------+---------+
ThrLeuLeuPheAsnIleLeuGlyGlyTrpValAlaAlaGlnLeuAlaProProSerAla
                              790                         800

       2410                2430                2450
GCTTCGGCTTTCGTGGGCGCCGGCATCGCCGGTGCGGCTGTTGGCAGCATAGGCCTTGGG
---------+---------+---------+---------+---------+---------+
AlaSerAlaPheValGlyAlaGlyIleAlaGlyAlaAlaValGlySerIleGlyLeuGly
                              810                         820

       2470                2490                2510
AAGGTGCTTGTGGACATTCTGGCGGGTTATGGAGCAGGAGTGGCCGGCGCGCTCGTGGCC
---------+---------+---------+---------+---------+---------+
LysValLeuValAspIleLeuAlaGlyTyrGlyAlaGlyValAlaGlyAlaLeuValAla
                              830                         840
```

FIG. 5F

```
        2530                2550                2570
TTCAAGGTCATGAGCGGCGAGATGCCCTCCACCGAGGACCTGGTCAATCTACTTCCTGCC
---------+---------+---------+---------+---------+---------+
PheLysValMetSerGlyGluMetProSerThrGluAspLeuValAsnLeuLeuProAla
                             850                           860

        2590                2610                2630
ATCCTCTCTCCTGGCGCCCTGGTCGTCGGGGTCGTGTGTGCAGCAATACTGCGTCGACAC
---------+---------+---------+---------+---------+---------+
IleLeuSerProGlyAlaLeuValValGlyValValCysAlaAlaIleLeuArgArgHis
                             870                           880

        2650                2670                2690
GTGGGTCCGGGAGAGGGGGCTGTGCAGTGGATGAACCGGCTGATAGCGTTCGCCTCGCGG
---------+---------+---------+---------+---------+---------+
ValGlyProGlyGluGlyAlaValGlnTrpMetAsnArgLeuIleAlaPheAlaSerArg
                             890                           900

        2710                2730                2750
GGTAATCATGTTTCCCCCACGCACTATGTGCCTGAGAGCGACGCCGCAGCGCGTGTTACT
---------+---------+---------+---------+---------+---------+
GlyAsnHisValSerProThrHisTyrValProGluSerAspAlaAlaAlaArgValThr
                             910                           920

        2770                2790                2810
CAGATCCTCTCCAGCCTTACCATCACTCAGCTGCTGAAAAGGCTCCACCAGTGGATTAAT
---------+---------+---------+---------+---------+---------+
GlnIleLeuSerSerLeuThrIleThrGlnLeuLeuLysArgLeuHisGlnTrpIleAsn
                             930                           940

        2830                2850                2870
GAAGACTGCTCCACACCGTGTTCCGGCTCGTGGCTAAGGGATGTTTGGGACTGGATATGC
---------+---------+---------+---------+---------+---------+
GluAspCysSerThrProCysSerGlySerTrpLeuArgAspValTrpAspTrpIleCys
                             950                           960

        2890                2910                2930
ACGGTGTTGACTGACTTCAAGACCTGGCTCCAGTCCAAGCTCCTGCCGCAGCTACCGGGA
---------+---------+---------+---------+---------+---------+
ThrValLeuThrAspPheLysThrTrpLeuGlnSerLysLeuLeuProGlnLeuProGly
                             970                           980
```

FIG. 5G

```
        2950                2970                2990
GTCCCTTTTTTCTCGTGCCAACGCGGGTACAAGGGAGTCTGGCGGGGAGACGGCATCATG
---------+---------+---------+---------+---------+---------+
ValProPhePheSerCysGlnArgGlyTyrLysGlyValTrpArgGlyAspGlyIleMet
                               990                          1000

        3010                3030                3050
CAAACCACCTGCCCATGTGGAGCACAGATCACCGGACATGTCAAAAACGGTTCCATGAGG
---------+---------+---------+---------+---------+---------+
GlnThrThrCysProCysGlyAlaGlnIleThrGlyHisValLysAsnGlySerMetArg
                              1010                          1020

        3070                3090                3110
ATCGTCGGGCCTAAGACCTGCAGCAACACGTGGCATGGAACATTCCCCATCAACGCATAC
---------+---------+---------+---------+---------+---------+
IleValGlyProLysThrCysSerAsnThrTrpHisGlyThrPheProIleAsnAlaTyr
                              1030                          1040

        3130                3150                3170
ACCACGGGCCCCTGCACACCCTCTCCAGCGCCAAACTATTCTAGGGCGCTGTGGCGGGTG
---------+---------+---------+---------+---------+---------+
ThrThrGlyProCysThrProSerProAlaProAsnTyrSerArgAlaLeuTrpArgVal
                              1050                          1060

        3190                3210                3230
GCCGCTGAGGAGTACGTGGAGGTCACGCGGGTGGGGGATTTCCACTACGTGACGGGCATG
---------+---------+---------+---------+---------+---------+
AlaAlaGluGluTyrValGluValThrArgValGlyAspPheHisTyrValThrGlyMet
                              1070                          1080

        3250                3270                3290
ACCACTGACAACGTAAAGTGCCCATGCCAGGTTCCGGCTCCTGAATTCTTCACGGAGGTG
---------+---------+---------+---------+---------+---------+
ThrThrAspAsnValLysCysProCysGlnValProAlaProGluPhePheThrGluVal
                              1090                          1100

        3310                3330                3350
GACGGAGTGCGGTTGCACAGGTACGCTCCGGCGTGCAGGCCTCTCCTACGGGAGGAGGTT
---------+---------+---------+---------+---------+---------+
AspGlyValArgLeuHisArgTyrAlaProAlaCysArgProLeuLeuArgGluGluVal
                              1110                          1120
```

FIG. 5H

```
        3370                3390                3410
ACATTCCAGGTCGGGCTCAACCAATACCTGGTTGGGTCACAGCTACCATGCGAGCCCGAA
---------+---------+---------+---------+---------+---------+
ThrPheGlnValGlyLeuAsnGlnTyrLeuValGlySerGlnLeuProCysGluProGlu
                            1130                          1140

        3430                3450                3470
CCGGATGTAGCAGTGCTCACTTCCATGCTCACCGACCCCTCCCACATCACAGCAGAAACG
---------+---------+---------+---------+---------+---------+
ProAspValAlaValLeuThrSerMetLeuThrAspProSerHisIleThrAlaGluThr
                            1150                          1160

        3490                3510                3530
GCTAAGCGTAGGTTGGCCAGGGGGTCTCCCCCCTCCTTGGCCAGCTCTTCAGCTAGCCAG
---------+---------+---------+---------+---------+---------+
AlaLysArgArgLeuAlaArgGlySerProProSerLeuAlaSerSerSerAlaSerGln
                            1170                          1180

        3550                3570                3590
TTGTCTGCGCCTTCCTTGAAGGCGACATGCACTACCCACCATGTCTCTCCGGACGCTGAC
---------+---------+---------+---------+---------+---------+
LeuSerAlaProSerLeuLysAlaThrCysThrThrHisHisValSerProAspAlaAsp
                            1190                          1200

        3610                3630                3650
CTCATCGAGGCCAACCTCCTGTGGCGGCAGGAGATGGGCGGGAACATCACCCGCGTGGAG
---------+---------+---------+---------+---------+---------+
LeuIleGluAlaAsnLeuLeuTrpArgGlnGluMetGlyGlyAsnIleThrArgValGlu
                            1210                          1220

        3670                3690                3710
TCGGAGAACAAGGTGGTAGTCCTGGACTCTTTCGACCCGCTTCGAGCGGAGGAGGATGAG
---------+---------+---------+---------+---------+---------+
SerGluAsnLysValValValLeuAspSerPheAspProLeuArgAlaGluGluAspGlu
                            1230                          1240

        3730                3750                3770
AGGGAAGTATCCGTTCCGGCGGAGATCCTGCGGAAATCCAAGAAGTTCCCCGCAGCGATG
---------+---------+---------+---------+---------+---------+
ArgGluValSerValProAlaGluIleLeuArgLysSerLysLysPheProAlaAlaMet
                            1250                          1260
```

FIG. 5I

```
        3790                3810                3830
CCCATCTGGGCGCGCCCGGATTACAACCCTCCACTGTTAGAGTCCTGGAAGGACCCGGAC
---------+---------+---------+---------+---------+---------+
ProIleTrpAlaArgProAspTyrAsnProProLeuLeuGluSerTrpLysAspProAsp
                    1270                          1280

        3850                3870                3890
TACGTCCCTCCGGTGGTGCACGGGTGCCCGTTGCCACCTATCAAGGCCCCTCCAATACCA
---------+---------+---------+---------+---------+---------+
TyrValProProValValHisGlyCysProLeuProProIleLysAlaProProIlePro
                    1290                          1300

        3910                3930                3950
CCTCCACGGAGAAAGAGGACGGTTGTCCTAACAGAGTCCTCCGTGTCTTCTGCCTTAGCG
---------+---------+---------+---------+---------+---------+
ProProArgArgLysArgThrValValLeuThrGluSerSerValSerSerAlaLeuAla
                    1310                          1320

        3970                3990                4010
GAGCTCGCTACTAAGACCTTCGGCAGCTCCGAATCATCGGCCGTCGACAGCGGCACGGCG
---------+---------+---------+---------+---------+---------+
GluLeuAlaThrLysThrPheGlySerSerGluSerSerAlaValAspSerGlyThrAla
                    1330                          1340

        4030                4050                4070
ACCGCCCTTCCTGACCAGGCCTCCGACGACGGTGACAAAGGATCCGACGTTGAGTCGTAC
---------+---------+---------+---------+---------+---------+
ThrAlaLeuProAspGlnAlaSerAspAspGlyAspLysGlySerAspValGluSerTyr
                    1350                          1360

        4090                4110                4130
TCCTCCATGCCCCCCCTTGAGGGGGAACCGGGGGACCCCGATCTCAGTGACGGGTCTTGG
---------+---------+---------+---------+---------+---------+
SerSerMetProProLeuGluGlyGluProGlyAspProAspLeuSerAspGlySerTrp
                    1370                          1380

        4150                4170                4190
TCTACCGTGAGCGAGGAAGCTAGTGAGGATGTCGTCTGCTGCTCAATGTCCTACACATGG
---------+---------+---------+---------+---------+---------+
SerThrValSerGluGluAlaSerGluAspValValCysCysSerMetSerTyrThrTrp
                    1390                          1400
```

FIG. 5J

```
        4210                4230                4250
ACAGGCGCCTTGATCACGCCATGCGCTGCGGAGGAAAGCAAGCTGCCCATCAACGCGTTG
---------+---------+---------+---------+---------+---------+
ThrGlyAlaLeuIleThrProCysAlaAlaGluGluSerLysLeuProIleAsnAlaLeu
                    1410                          1420

        4270                4290                4310
AGCAACTCTTTGCTGCGCCACCATAACATGGTTTATGCCACAACATCTCGCAGCGCAGGC
---------+---------+---------+---------+---------+---------+
SerAsnSerLeuLeuArgHisHisAsnMetValTyrAlaThrThrSerArgSerAlaGly
                    1430                          1440

        4330                4350                4370
CTGCGGCAGAAGAAGGTCACCTTTGACAGACTGCAAGTCCTGGACGACCACTACCGGGAC
---------+---------+---------+---------+---------+---------+
LeuArgGlnLysLysValThrPheAspArgLeuGlnValLeuAspAspHisTyrArgAsp
                    1450                          1460

        4390                4410                4430
GTGCTCAAGGAGATGAAGGCGAAGGCGTCCACAGTTAAGGCTAAACTCCTATCCGTAGAG
---------+---------+---------+---------+---------+---------+
ValLeuLysGluMetLysAlaLysAlaSerThrValLysAlaLysLeuLeuSerValGlu
                    1470                          1480

        4450                4470                4490
GAAGCCTGCAAGCTGACGCCCCCACATTCGGCCAAATCCAAGTTTGGCTATGGGGCAAAG
---------+---------+---------+---------+---------+---------+
GluAlaCysLysLeuThrProProHisSerAlaLysSerLysPheGlyTyrGlyAlaLys
                    1490                          1500

        4510                4530                4550
GACGTCCGGAACCTATCCAGCAAGGCCGTTAACCACATCCACTCCGTGTGGAAGGACTTG
---------+---------+---------+---------+---------+---------+
AspValArgAsnLeuSerSerLysAlaValAsnHisIleHisSerValTrpLysAspLeu
                    1510                          1520

        4570                4590                4610
CTGGAAGACACTGTGACACCAATTGACACCACCATCATGGCAAAAAATGAGGTTTTCTGT
---------+---------+---------+---------+---------+---------+
LeuGluAspThrValThrProIleAspThrThrIleMetAlaLysAsnGluValPheCys
                    1530                          1540
```

FIG. 5K

```
        4630                4650                4670
GTCCAACCAGAGAAAGGAGGCCGTAAGCCAGCCCGCCTTATCGTATTCCCAGATCTGGGA
---------+---------+---------+---------+---------+---------+
ValGlnProGluLysGlyGlyArgLysProAlaArgLeuIleValPheProAspLeuGly
                    1550                          1560

        4690                4710                4730
GTCCGTGTATGCGAGAAGATGGCCCTCTATGATGTGGTCTCCACCCTTCCTCAGGTCGTG
---------+---------+---------+---------+---------+---------+
ValArgValCysGluLysMetAlaLeuTyrAspValValSerThrLeuProGlnValVal
                    1570                          1580

        4750                4770                4790
ATGGGCTCCTCATACGGATTCCAGTACTCTCCTGGGCAGCGAGTCGAGTTCCTGGTGAAT
---------+---------+---------+---------+---------+---------+
MetGlySerSerTyrGlyPheGlnTyrSerProGlyGlnArgValGluPheLeuValAsn
                    1590                          1600

        4810                4830                4850
ACCTGGAAATCAAAGAAAAACCCCATGGGCTTTTCATATGACACTCGCTGTTTCGACTCA
---------+---------+---------+---------+---------+---------+
ThrTrpLysSerLysLysAsnProMetGlyPheSerTyrAspThrArgCysPheAspSer
                    1610                          1620

        4870                4890                4910
ACGGTCACCGAGAACGACATCCGTGTTGAGGAGTCAATTTACCAATGTTGTGACTTGGCC
---------+---------+---------+---------+---------+---------+
ThrValThrGluAsnAspIleArgValGluGluSerIleTyrGlnCysCysAspLeuAla
                    1630                          1640

        4930                4950                4970
CCCGAAGCCAGACAGGCCATAAAATCGCTCACAGAGCGGCTTTATATCGGGGGTCCTCTG
---------+---------+---------+---------+---------+---------+
ProGluAlaArgGlnAlaIleLysSerLeuThrGluArgLeuTyrIleGlyGlyProLeu
                    1650                          1660

        4990                5010                5030
ACTAATTCAAAAGGGCAGAACTGCGGTTATCGCCGGTGCCGCGCGAGCGGCGTGCTGACG
---------+---------+---------+---------+---------+---------+
ThrAsnSerLysGlyGlnAsnCysGlyTyrArgArgCysArgAlaSerGlyValLeuThr
                    1670                          1680
```

FIG. 5L

```
        5050                5070                5090
ACTAGCTGCGGTAACACCCTCACATGTTACTTGAAGGCCTCTGCAGCCTGTCGAGCTGCG
---------+---------+---------+---------+---------+---------+
ThrSerCysGlyAsnThrLeuThrCysTyrLeuLysAlaSerAlaAlaCysArgAlaAla
                            1690                          1700

        5110                5130                5150
AAGCTCCAGGACTGCACGATGCTCGTGAACGGAGACGACCTTGTCGTTATCTGTGAAAGC
---------+---------+---------+---------+---------+---------+
LysLeuGlnAspCysThrMetLeuValAsnGlyAspAspLeuValValIleCysGluSer
                            1710                          1720

        5170                5190                5210
GCGGGAACCCAAGAGGACGCGGCGAGCCTACGAGTCTTCACGGAGGCTATGACTAGGTAC
---------+---------+---------+---------+---------+---------+
AlaGlyThrGlnGluAspAlaAlaSerLeuArgValPheThrGluAlaMetThrArgTyr
                            1730                          1740

        5230                5250                5270
TCTGCCCCCCCCGGGGACCCGCCCCAACCAGAATACGACTTGGAGCTGATAACATCATGT
---------+---------+---------+---------+---------+---------+
SerAlaProProGlyAspProProGlnProGluTyrAspLeuGluLeuIleThrSerCys
                            1750                          1760

        5290                5310                5330
TCCTCCAATGTGTCGGTCGCCCACGATGCATCAGGCAAAAGGGTGTACTACCTCACCCGT
---------+---------+---------+---------+---------+---------+
SerSerAsnValSerValAlaHisAspAlaSerGlyLysArgValTyrTyrLeuThrArg
                            1770                          1780

        5350                5370                5390
GATCCCACCACCCCCCTCGCACGGGCTGCGTGGGAAACAGCTAGACACACTCCAGTTAAC
---------+---------+---------+---------+---------+---------+
AspProThrThrProLeuAlaArgAlaAlaTrpGluThrAlaArgHisThrProValAsn
                            1790                          1800

        5410                5430                5450
TCCTGGCTAGGCAACATTATCATGTATGCGCCCACTTTGTGGGCAAGGATGATTCTGATG
---------+---------+---------+---------+---------+---------+
SerTrpLeuGlyAsnIleIleMetTyrAlaProThrLeuTrpAlaArgMetIleLeuMet
                            1810                          1820
```

FIG. 5M

```
        5470                5490                5510
ACTCACTTCTTCTCCATCCTTCTAGCACAGGAGCAACTTGAAAAAGCCCTGGACTGCCAG
---------+---------+---------+---------+---------+---------+
ThrHisPhePheSerIleLeuLeuAlaGlnGluGlnLeuGluLysAlaLeuAspCysGln
                            1830                          1840

        5530                5550                5570
ATCTACGGGGCCTGTTACTCCATTGAGCCACTTGACCTACCTCAGATCATTGAACGACTC
---------+---------+---------+---------+---------+---------+
IleTyrGlyAlaCysTyrSerIleGluProLeuAspLeuProGlnIleIleGluArgLeu
                            1850                          1860

        5590                5610                5630
CATGGCCTTAGCGCATTTTCACTCCATAGTTACTCTCCAGGTGAGATCAATAGGGTGGCT
---------+---------+---------+---------+---------+---------+
HisGlyLeuSerAlaPheSerLeuHisSerTyrSerProGlyGluIleAsnArgValAla
                            1870                          1880

        5650                5670                5690
TCATGCCTCAGGAAACTTGGGGTACCACCCTTGCGAGTCTGGAGACATCGGGCCAGGAGC
---------+---------+---------+---------+---------+---------+
SerCysLeuArgLysLeuGlyValProProLeuArgValTrpArgHisArgAlaArgSer
                            1890                          1900

        5710                5730                5750
GTCCGCGCTAGGCTACTGTCCCAGGGGGGGAGGGCCGCCACTTGTGGCAAGTACCTCTTC
---------+---------+---------+---------+---------+---------+
ValArgAlaArgLeuLeuSerGlnGlyGlyArgAlaAlaThrCysGlyLysTyrLeuPhe
                            1910                          1920

        5770                5790                5810
AACTGGGCAGTGAAGACCAAACTCAAACTCACTCCAATCCCGGCTGCGTCCCAGCTGGAC
---------+---------+---------+---------+---------+---------+
AsnTrpAlaValLysThrLysLeuLysLeuThrProIleProAlaAlaSerGlnLeuAsp
                            1930                          1940

        5830                5850                5870
TTGTCCGGCTGGTTCGTTGCTGGTTACAGCGGGGGAGACATATATCACAGCCTGTCTCGT
---------+---------+---------+---------+---------+---------+
LeuSerGlyTrpPheValAlaGlyTyrSerGlyGlyAspIleTyrHisSerLeuSerArg
                            1950                          1960
```

FIG. 5N

```
     5890                5910                5930
GCCCGACCCCGCTGGTTCATGCTGTGCCTACTCCTACTTTCTGTAGGGGTAGGCATCTAC
---------+---------+---------+---------+---------+---------+
AlaArgProArgTrpPheMetLeuCysLeuLeuLeuLeuSerValGlyValGlyIleTyr
                          1970                        1980

     5950 5955
CTGCTCCCCAACCGA   (SEQ. ID. NO. 5)
---------+-----
LeuLeuProAsnArg   (SEQ. ID. NO. 6)
          1985
```

FIG. 5O

1	TCGCGCGTTT	CGGTGATGAC	GGTGAAAACC	TCTGACACAT	GCAGCTCCCG
51	GAGACGGTCA	CAGCTTGTCT	GTAAGCGGAT	GCCGGGAGCA	GACAAGCCCG
101	TCAGGGCGCG	TCAGCGGGTG	TTGGCGGGTG	TCGGGGCTGG	CTTAACTATG
151	CGGCATCAGA	GCAGATTGTA	CTGAGAGTGC	ACCATATGCG	GTGTGAAATA
201	CCGCACAGAT	GCGTAAGGAG	AAAATACCGC	ATCAGATTGG	CTATTGGCCA
251	TTGCATACGT	TGTATCCATA	TCATAATATG	TACATTTATA	TTGGCTCATG
301	TCCAACATTA	CCGCCATGTT	GACATTGATT	ATTGACTAGT	TATTAATAGT
351	AATCAATTAC	GGGGTCATTA	GTTCATAGCC	CATATATGGA	GTTCCGCGTT
401	ACATAACTTA	CGGTAAATGG	CCCGCCTGGC	TGACCGCCCA	ACGACCCCCG
451	CCCATTGACG	TCAATAATGA	CGTATGTTCC	CATAGTAACG	CCAATAGGGA
501	CTTTCCATTG	ACGTCAATGG	GTGGAGTATT	TACGGTAAAC	TGCCCACTTG
551	GCAGTACATC	AAGTGTATCA	TATGCCAAGT	ACGCCCCCTA	TTGACGTCAA
601	TGACGGTAAA	TGGCCCGCCT	GGCATTATGC	CCAGTACATG	ACCTTATGGG
651	ACTTTCCTAC	TTGGCAGTAC	ATCTACGTAT	TAGTCATCGC	TATTACCATG
701	GTGATGCGGT	TTTGGCAGTA	CATCAATGGG	CGTGGATAGC	GGTTTGACTC
751	ACGGGGATTT	CCAAGTCTCC	ACCCCATTGA	CGTCAATGGG	AGTTTGTTTT
801	GGCACCAAAA	TCAACGGGAC	TTTCCAAAAT	GTCGTAACAA	CTCCGCCCCA
851	TTGACGCAAA	TGGGCGGTAG	GCGTGTACGG	TGGGAGGTCT	ATATAAGCAG
901	AGCTCGTTTA	GTGAACCGTC	AGATCGCCTG	GAGACGCCAT	CCACGCTGTT
951	TTGACCTCCA	TAGAAGACAC	CGGGACCGAT	CCAGCCTCCG	CGGCCGGGAA
1001	CGGTGCATTG	GAACGCGGAT	TCCCCGTGCC	AAGAGTGACG	TAAGTACCGC
1051	CTATAGACTC	TATAGGCACA	CCCCTTTGGC	TCTTATGCAT	GCTATACTGT
1101	TTTTGGCTTG	GGGCCTATAC	ACCCCCGCTT	CCTTATGCTA	TAGGTGATGG
1151	TATAGCTTAG	CCTATAGGTG	TGGGTTATTG	ACCATTATTG	ACCACTCCCC
1201	TATTGGTGAC	GATACTTTCC	ATTACTAATC	CATAACATGG	CTCTTTGCCA
1251	CAACTATCTC	TATTGGCTAT	ATGCCAATAC	TCTGTCCTTC	AGAGACTGAC
1301	ACGGACTCTG	TATTTTTACA	GGATGGGGTC	CCATTTATTA	TTTACAAATT
1351	CACATATACA	ACAACGCCGT	CCCCCGTGCC	CGCAGTTTTT	ATTAAACATA
1401	GCGTGGGATC	TCCACGCGAA	TCTCGGGTAC	GTGTTCCGGA	CATGGGCTCT
1451	TCTCCGGTAG	CGGCGGAGCT	TCCACATCCG	AGCCCTGGTC	CCATGCCTCC
1501	AGCGGCTCAT	GGTCGCTCGG	CAGCTCCTTG	CTCCTAACAG	TGGAGGCCAG
1551	ACTTAGGCAC	AGCACAATGC	CCACCACCAC	CAGTGTGCCG	CACAAGGCCG
1601	TGGCGGTAGG	GTATGTGTCT	GAAAATGAGC	GTGGAGATTG	GGCTCGCACG
1651	GCTGACGCAG	ATGGAAGACT	TAAGGCAGCG	GCAGAAGAAG	ATGCAGGCAG
1701	CTGAGTTGTT	GTATTCTGAT	AAGAGTCAGA	GGTAACTCCC	GTTGCGGTGC
1751	TGTTAACGGT	GGAGGGCAGT	GTAGTCTGAG	CAGTACTCGT	TGCTGCCGCG
1801	CGCGCCACCA	GACATAATAG	CTGACAGACT	AACAGACTGT	TCCTTTCCAT
1851	GGGTCTTTTC	TGCAGTCACC	GTCCTTAGAT	CTAGGTACCA	GATATCAGAA
1901	TTCAGTCGAC	AGCGGCCGCG	ATCTGCTGTG	CCTTCTAGTT	GCCAGCCATC
1951	TGTTGTTTGC	CCCTCCCCCG	TGCCTTCCTT	GACCCTGGAA	GGTGCCACTC
2001	CCACTGTCCT	TTCCTAATAA	AATGAGGAAA	TTGCATCGCA	TTGTCTGAGT
2051	AGGTGTCATT	CTATTCTGGG	GGGTGGGGTG	GGGCAGGACA	GCAAGGGGGA

FIG. 6A

2101	GGATTGGGAA	GACAATAGCA	GGCATGCTGG	GGATGCGGTG	GGCTCTATGG
2151	CCGCTGCGGC	CAGGTGCTGA	AGAATTGACC	CGGTTCCTCC	TGGGCCAGAA
2201	AGAAGCAGGC	ACATCCCCTT	CTCTGTGACA	CACCCTGTCC	ACGCCCCTGG
2251	TTCTTAGTTC	CAGCCCCACT	CATAGGACAC	TCATAGCTCA	GGAGGGCTCC
2301	GCCTTCAATC	CCACCCGCTA	AAGTACTTGG	AGCGGTCTCT	CCCTCCCTCA
2351	TCAGCCCACC	AAACCAAACC	TAGCCTCCAA	GAGTGGGAAG	AAATTAAAGC
2401	AAGATAGGCT	ATTAAGTGCA	GAGGGAGAGA	AAATGCCTCC	AACATGTGAG
2451	GAAGTAATGA	GAGAAATCAT	AGAATTTCTT	CCGCTTCCTC	GCTCACTGAC
2501	TCGCTGCGCT	CGGTCGTTCG	GCTGCGGCGA	GCGGTATCAG	CTCACTCAAA
2551	GGCGGTAATA	CGGTTATCCA	CAGAATCAGG	GGATAACGCA	GGAAAGAACA
2601	TGTGAGCAAA	AGGCCAGCAA	AAGGCCAGGA	ACCGTAAAAA	GGCCGCGTTG
2651	CTGGCGTTTT	TCCATAGGCT	CCGCCCCCCT	GACGAGCATC	ACAAAAATCG
2701	ACGCTCAAGT	CAGAGGTGGC	GAAACCCGAC	AGGACTATAA	AGATACCAGG
2751	CGTTTCCCCC	TGGAAGCTCC	CTCGTGCGCT	CTCCTGTTCC	GACCCTGCCG
2801	CTTACCGGAT	ACCTGTCCGC	CTTTCTCCCT	TCGGGAAGCG	TGGCGCTTTC
2851	TCATAGCTCA	CGCTGTAGGT	ATCTCAGTTC	GGTGTAGGTC	GTTCGCTCCA
2901	AGCTGGGCTG	TGTGCACGAA	CCCCCCGTTC	AGCCCGACCG	CTGCGCCTTA
2951	TCCGGTAACT	ATCGTCTTGA	GTCCAACCCG	GTAAGACACG	ACTTATCGCC
3001	ACTGGCAGCA	GCCACTGGTA	ACAGGATTAG	CAGAGCGAGG	TATGTAGGCG
3051	GTGCTACAGA	GTTCTTGAAG	TGGTGGCCTA	ACTACGGCTA	CACTAGAAGA
3101	ACAGTATTTG	GTATCTGCGC	TCTGCTGAAG	CCAGTTACCT	TCGGAAAAAG
3151	AGTTGGTAGC	TCTTGATCCG	GCAAACAAAC	CACCGCTGGT	AGCGGTGGTT
3201	TTTTTGTTTG	CAAGCAGCAG	ATTACGCGCA	GAAAAAAAGG	ATCTCAAGAA
3251	GATCCTTTGA	TCTTTTCTAC	GGGGTCTGAC	GCTCAGTGGA	ACGAAAACTC
3301	ACGTTAAGGG	ATTTTGGTCA	TGAGATTATC	AAAAAGGATC	TTCACCTAGA
3351	TCCTTTTAAA	TTAAAAATGA	AGTTTTAAAT	CAATCTAAAG	TATATATGAG
3401	TAAACTTGGT	CTGACAGTTA	CCAATGCTTA	ATCAGTGAGG	CACCTATCTC
3451	AGCGATCTGT	CTATTTCGTT	CATCCATAGT	TGCCTGACTC	GGGGGGGGGG
3501	GGCGCTGAGG	TCTGCCTCGT	GAAGAAGGTG	TTGCTGACTC	ATACCAGGCC
3551	TGAATCGCCC	CATCATCCAG	CCAGAAAGTG	AGGGAGCCAC	GGTTGATGAG
3601	AGCTTTGTTG	TAGGTGGACC	AGTTGGTGAT	TTTGAACTTT	TGCTTTGCCA
3651	CGGAACGGTC	TGCGTTGTCG	GGAAGATGCG	TGATCTGATC	CTTCAACTCA
3701	GCAAAAGTTC	GATTTATTCA	ACAAAGCCGC	CGTCCCGTCA	AGTCAGCGTA
3751	ATGCTCTGCC	AGTGTTACAA	CCAATTAACC	AATTCTGATT	AGAAAAACTC
3801	ATCGAGCATC	AAATGAAACT	GCAATTTATT	CATATCAGGA	TTATCAATAC
3851	CATATTTTTG	AAAAAGCCGT	TTCTGTAATG	AAGGAGAAAA	CTCACCGAGG
3901	CAGTTCCATA	GGATGGCAAG	ATCCTGGTAT	CGGTCTGCGA	TTCCGACTCG
3951	TCCAACATCA	ATACAACCTA	TTAATTTCCC	CTCGTCAAAA	ATAAGGTTAT
4001	CAAGTGAGAA	ATCACCATGA	GTGACGACTG	AATCCGGTGA	GAATGGCAAA
4051	AGCTTATGCA	TTTCTTTCCA	GACTTGTTCA	ACAGGCCAGC	CATTACGCTC
4101	GTCATCAAAA	TCACTCGCAT	CAACCAAACC	GTTATTCATT	CGTGATTGCG
4151	CCTGAGCGAG	ACGAAATACG	CGATCGCTGT	TAAAAGGACA	ATTACAAACA

FIG. 6B

4201 GGAATCGAAT GCAACCGGCG CAGGAACACT GCCAGCGCAT CAACAATATT
4251 TTCACCTGAA TCAGGATATT CTTCTAATAC CTGGAATGCT GTTTTCCCGG
4301 GGATCGCAGT GGTGAGTAAC CATGCATCAT CAGGAGTACG GATAAAATGC
4351 TTGATGGTCG GAAGAGGCAT AAATTCCGTC AGCCAGTTTA GTCTGACCAT
4401 CTCATCTGTA ACATCATTGG CAACGCTACC TTTGCCATGT TTCAGAAACA
4451 ACTCTGGCGC ATCGGGCTTC CCATACAATC GATAGATTGT CGCACCTGAT
4501 TGCCCGACAT TATCGCGAGC CCATTTATAC CCATATAAAT CAGCATCCAT
4551 GTTGGAATTT AATCGCGGCC TCGAGCAAGA CGTTTCCCGT TGAATATGGC
4601 TCATAACACC CCTTGTATTA CTGTTTATGT AAGCAGACAG TTTTATTGTT
4651 CATGATGATA TATTTTTATC TTGTGCAATG TAACATCAGA GATTTTGAGA
4701 CACAACGTGG CTTTCCCCCC CCCCCCATTA TTGAAGCATT TATCAGGGTT
4751 ATTGTCTCAT GAGCGGATAC ATATTTGAAT GTATTTAGAA AAATAAACAA
4801 ATAGGGGTTC CGCGCACATT TCCCCGAAAA GTGCCACCTG ACGTCTAAGA
4851 AACCATTATT ATCATGACAT TAACCTATAA AAATAGGCGT ATCACGAGGC
4901 CCTTTCGTC

FIG. 6C

```
1    CATCATCAAT AATATACCTT ATTTTGGATT GAAGCCAATA TGATAATGAG GGGGTGGAGT
61   TTGTGACGTG GCGCGGGGCG TGGGAACGGG GCGGGTGACG TAGTAGTGTG GCGGAAGTGT
121  GATGTTGTAA GTGTGGCGGA ACACATGTAA GCGCCGGATG TGGTAAAAGT GACGTTTTTG
181  GTGTGCGCCG GTGTACACGG GAAGTGACAA TTTTCGCGCG GTTTTAGGCG GATGTTGTAG
241  TAAATTTGGG CGTAACCAAG TAATATTTGG CCATTTTCGC GGGAAAACTG AATAAGAGGA
301  AGTGAAATCT GAATAATTCT GTGTTACTCA TAGCGCGTAA TATTTGTCTA GGGCCGCGGG
361  GACTTTGACC GTTTACGTGG AGACTCGCCC AGGTGTTTTT CTCAGGTGTT TTCCGCGTTC
421  CGGGTCAAAG TTGGCGTTTT ATTATTATAG TCAGCTGACG CGCAGTGTAT TTATACCCGG
481  TGAGTTCCTC AAGAGGCCAC TCTTGAGTGC CAGCGAGTAG AGTTTTCTCC TCCGAGCCGC
541  TCCGACACCG GGACTGAAAA TGAGACATAT TATCTGCCAC GGAGGTGTTA TTACCGAAGA
601  AATGGCCGCC AGTCTTTTGG ACCAGCTGAT CGAAGAGGTA CTGGCTGATA ATCTTCCACC
661  TCCTAGCCAT TTTGAACCAC CTACCCTTCA CGAACTGTAT GATTTAGACG TGACGGCCCC
721  CGAAGATCCC AACGAGGAGG CGGTTTCGCA GATTTTTCCC GAGTCTGTAA TGTTGGCGGT
781  GCAGGAAGGG ATTGACTTAT TCACTTTTCC GCCGGCGCCC GGTTCTCCGG AGCCGCCTCA
841  CCTTTCCCGG CAGCCCGAGC AGCCGGAGCA GAGAGCCTTG GGTCCGGTTT CTATGCCAAA
901  CCTTGTGCCG GAGGTGATCG ATCTTACCTG CCACGAGGCT GGCTTTCCAC CCAGTGACGA
961  CGAGGATGAA GAGGGTGAGG AGTTTGTGTT AGATTATGTG GAGCACCCCG GGCACGGTTG
1021 CAGGTCTTGT CATTATCACC GGAGGAATAC GGGGGACCCA GATATTATGT GTTCGCTTTG
1081 CTATATGAGG ACCTGTGGCA TGTTTGTCTA CAGTAAGTGA AAAATTATGG GCAGTGGGTG
1141 ATAGAGTGGT GGGTTTGGTG TGGTAATTTT TTTTTTAATT TTTACAGTTT TGTGGTTTAA
1201 AGAATTTTGT ATTGTGATTT TTTAAAAGGT CCTGTGTCTG AACCTGAGCC TGAGCCCGAG
1261 CCAGAACCGG AGCCTGCAAG ACCTACCCGG CGTCCTAAAT TGGTGCCTGC TATCCTGAGA
1321 CGCCCGACAT CACCTGTGTC TAGAGAATGC AATAGTAGTA CGGATAGCTG TGACTCCGGT
1381 CCTTCTAACA CACCTCCTGA GATACACCCG GTGGTCCCGC TGTGCCCCAT TAAACCAGTT
1441 GCCGTGAGAG TTGGTGGGCG TCGCCAGGCT GTGGAATGTA TCGAGGACTT GCTTAACGAG
1501 TCTGGGCAAC CTTTGGACTT GAGCTGTAAA CGCCCCAGGC CATAAGGTGT AAACCTGTGA
1561 TTGCGTGTGT GGTTAACGCC TTTGTTTGCT GAATGAGTTG ATGTAAGTTT AATAAAGGGT
1621 GAGATAATGT TTAACTTGCA TGGCGTGTTA AATGGGGCGG GGCTTAAAGG GTATATAATG
1681 CGCCGTGGGC TAATCTTGGT TACATCTGAC CTCATGGAGG CTTGGGAGTG TTTGGAAGAT
1741 TTTTCTGCTG TGCGTAACTT GCTGGAACAG AGCTCTAACA GTACCTCTTG GTTTTGGAGG
1801 TTTCTGTGGG GCTCCTCCCA GGCAAAGTTA GTCTGCAGAA TTAAGGAGGA TTACAAGTGG
1861 GAATTTGAAG AGCTTTTGAA ATCCTGTGGT GAGCTGTTTG ATTCTTTGAA TCTGGGTCAC
1921 CAGGCGCTTT TCCAAGAGAA GGTCATCAAG ACTTTGGATT TTTCCACACC GGGGCGCGCT
1981 GCGGCTGCTG TTGCTTTTTT GAGTTTTATA AAGGATAAAT GGAGCGAAGA AACCCATCTG
2041 AGCGGGGGGT ACCTGCTGGA TTTTCTGGCC ATGCATCTGT GGAGAGCGGT GGTGAGACAC
2101 AAGAATCGCC TGCTACTGTT GTCTTCCGTC CGCCCGGCAA TAATACCGAC GGAGGAGCAA
2161 CAGCAGGAGG AAGCCAGGCG GCGGCGGCGG CAGGAGCAGA GCCCATGGAA CCCGAGAGCC
2221 GGCCTGGACC CTCGGGAATG AATGTTGTAC AGGTGGCTGA ACTGTTTCCA GAACTGAGAC
2281 GCATTTTAAC CATTAACGAG GATGGGCAGG GGCTAAAGGG GGTAAAGAAG GAGCGGGGGG
2341 CTTCTGAGGC TACAGAGGAG GCTAGGAATC TAACTTTTAG CTTAATGACC AGACACCGTC
2401 CTGAGTGTGT TACTTTTCAG CAGATTAAGG ATAATTGCGC TAATGAGCTT GATCTGCTGG
2461 CGCAGAAGTA TTCCATAGAG CAGCTGACCA CTTACTGGCT GCAGCCAGGG GATGATTTTG
```

FIG. 7A

2521 AGGAGGCTAT TAGGGTATAT GCAAAGGTGG CACTTAGGCC AGATTGCAAG TACAAGATTA
2581 GCAAACTTGT AAATATCAGG AATTGTTGCT ACATTTCTGG GAACGGGGCC GAGGTGGAGA
2641 TAGATACGGA GGATAGGGTG GCCTTTAGAT GTAGCATGAT AAATATGTGG CCGGGGGTGC
2701 TTGGCATGGA CGGGGTGGTT ATTATGAATG TGAGGTTTAC TGGTCCCAAT TTTAGCGGTA
2761 CGGTTTTCCT GGCCAATACC AATCTTATCC TACACGGTGT AAGCTTCTAT GGGTTTAACA
2821 ATACCTGTGT GGAAGCCTGG ACCGATGTAA GGGTTCGGGG CTGTGCCTTT TACTGCTGCT
2881 GGAAGGGGGT GGTGTGTCGC CCCAAAAGCA GGGCTTCAAT TAAGAAATGC CTGTTTGAAA
2941 GGTGTACCTT GGGTATCCTG TCTGAGGGTA ACTCCAGGGT GCGCCACAAT GTGGCCTCCG
3001 ACTGTGGTTG CTTTATGCTA GTGAAAAGCG TGGCTGTGAT TAAGCATAAC ATGGTGTGTG
3061 GCAACTGCGA GGACAGGGCC TCTCAGATGC TGACCTGCTC GGACGGCAAC TGTCACTTGC
3121 TGAAGACCAT TCACGTAGCC AGCCACTCTC GCAAGGCCTG GCCAGTGTTT GAGCACAACA
3181 TACTGACCCG CTGTTCCTTG CATTTGGGTA ACAGGAGGGG GGTGTTCCTA CCTTACCAAT
3241 GCAATTTGAG TCACACTAAG ATATTGCTTG AGCCCGAGAG CATGTCCAAG GTGAACCTGA
3301 ACGGGGTGTT TGACATGACC ATGAAGATCT GGAAGGTGCT GAGGTACGAT GAGACCCGCA
3361 CCAGGTGCAG ACCCTGCGAG TGTGGCGGTA AACATATTAG GAACCAGCCT GTGATGCTGG
3421 ATGTGACCGA GGAGCTGAGG CCCGATCACT TGGTGCTGGC CTGCACCCGC GCTGAGTTTG
3481 GCTCTAGCGA TGAAGATACA GATTGAGGTA CTGAAATGTG TGGGCGTGGC TTAAGGGTGG
3541 GAAAGAATAT ATAAGGTGGG GGTCTCATGT AGTTTTGTAT CTGTTTTGCA GCAGCCGCCG
3601 CCATGAGCGC CAACTCGTTT GATGGAAGCA TTGTGAGCTC ATATTTGACA ACGCGCATGC
3661 CCCCATGGGC CGGGGTGCGT CAGAATGTGA TGGGCTCCAG CATTGATGGT CGCCCCGTCC
3721 TGCCCGCAAA CTCTACTACC TTGACCTACG AGACCGTGTC TGGAACGCCG TTGGAGACTG
3781 CAGCCTCCGC CGCCGCTTCA GCCGCTGCAG CCACCGCCCG CGGGATTGTG ACTGACTTTG
3841 CTTTCCTGAG CCCGCTTGCA AGCAGTGCAG CTTCCCGTTC ATCCGCCCGC GATGACAAGT
3901 TGACGGCTCT TTTGGCACAA TTGGATTCTT TGACCCGGGA ACTTAATGTC GTTTCTCAGC
3961 AGCTGTTGGA TCTGCGCCAG CAGGTTTCTG CCCTGAAGGC TTCCTCCCCT CCCAATGCGG
4021 TTTAAAACAT AAATAAAAAC CAGACTCTGT TTGGATTTGG ATCAAGCAAG TGTCTTGCTG
4081 TCTTTATTTA GGGGTTTTGC GCGCGCGGTA GGCCCGGGAC CAGCGGTCTC GGTCGTTGAG
4141 GGTCCTGTGT ATTTTTTCCA GGACGTGGTA AAGGTGACTC TGGATGTTCA GATACATGGG
4201 CATAAGCCCG TCTCTGGGGT GGAGGTAGCA CCACTGCAGA GCTTCATGCT GCGGGGTGGT
4261 GTTGTAGATG ATCCAGTCGT AGCAGGAGCG CTGGGCGTGG TGCCTAAAAA TGTCTTTCAG
4321 TAGCAAGCTG ATTGCCAGGG GCAGGCCCTT GGTGTAAGTG TTTACAAAGC GGTTAAGCTG
4381 GGATGGGTGC ATACGTGGGG ATATGAGATG CATCTTGGAC TGTATTTTTA GGTTGGCTAT
4441 GTTCCCAGCC ATATCCCTCC GGGGATTCAT GTTGTGCAGA ACCACCAGCA CAGTGTATCC
4501 GGTGCACTTG GGAAATTTGT CATGTAGCTT AGAAGGAAAT GCGTGGAAGA ACTTGGAGAC
4561 GCCCTTGTGA CCTCCAAGAT TTTCCATGCA TTCGTCCATA ATGATGGCAA TGGGCCCACG
4621 GGCGGCGGCC TGGGCGAAGA TATTTCTGGG ATCACTAACG TCATAGTTGT GTTCCAGGAT
4681 GAGATCGTCA TAGGCCATTT TTACAAAGCG CGGGCGGAGG GTGCCAGACT GCGGTATAAT
4741 GGTTCCATCC GGCCCAGGGG CGTAGTTACC CTCACAGATT TGCATTTCCC ACGCTTTGAG
4801 TTCAGATGGG GGGATCATGT CTACCTGCGG GGCGATGAAG AAAACCGTTT CCGGGGTAGG
4861 GGAGATCAGC TGGGAAGAAA GCAGGTTCCT AAGCAGCTGC GACTTACCGC AGCCGGTGGG
4921 CCCGTAAATC ACACCTATTA CCGGCTGCAA CTGGTAGTTA AGAGAGCTGC AGCTGCCGTC
4981 ATCCCTGAGC AGGGGGGCCA CTTCGTTAAG CATGTCCCTG ACTTGCATGT TTTCCCTGAC

FIG. 7B

5041 CAAATCCGCC AGAAGGCGCT CGCCGCCCAG CGATAGCAGT TCTTGCAAGG AAGCAAAGTT
5101 TTTCAACGGT TTGAGGCCGT CCGCCGTAGG CATGCTTTTG AGCGTTTGAC CAAGCAGTTC
5161 CAGGCGGTCC CACAGCTCGG TCACGTGCTC TACGGCATCT CGATCCAGCA TATCTCCTCG
5221 TTTCGCGGGT TGGGGCGGCT TTCGCTGTAC GGCAGTAGTC GGTGCTCGTC CAGACGGGCC
5281 AGGGTCATGT CTTTCCACGG GCGCAGGGTC CTCGTCAGCG TAGTCTGGGT CACGGTGAAG
5341 GGGTGCGCTC CGGGTTGCGC GCTGGCCAGG GTGCGCTTGA GGCTGGTCCT GCTGGTGCTG
5401 AAGCGCTGCC GGTCTTCGCC CTGCGCGTCG GCCAGGTAGC ATTTGACCAT GGTGTCATAG
5461 TCCAGCCCCT CCGCGGCGTG GCCCTTGGCG CGCAGCTTGC CCTTGGAGGA GGCGCCGCAC
5521 GAGGGGCAGT GCAGACTTTT AAGGGCGTAG AGCTTGGGCG CGAGAAATAC CGATTCCGGG
5581 GAGTAGGCAT CCGCGCCGCA GGCCCCGCAG ACGGTCTCGC ATTCCACGAG CCAGGTGAGC
5641 TCTGGCCGTT CGGGGTCAAA AACCAGGTTT CCCCCATGCT TTTTGATGCG TTTCTTACCT
5701 CTGGTTTCCA TGAGCCGGTG TCCACGCTCG GTGACGAAAA GGCTGTCCGT GTCCCCGTAT
5761 ACAGACTTGA GAGGCCTGTC CTCGAGCGGT GTTCCGCGGT CCTCCTCGTA TAGAAACTCG
5821 GACCACTCTG AGACGAAGGC TCGCGTCCAG GCCAGCACGA AGGAGGCTAA GTGGGAGGGG
5881 TAGCGGTCGT TGTCCACTAG GGGGTCCACT CGCTCCAGGG TGTGAAGACA CATGTCGCCC
5941 TCTTCGGCAT CAAGGAAGGT GATTGGTTTA TAGGTGTAGG CCACGTGACC GGGTGTTCCT
6001 GAAGGGGGGC TATAAAAGGG GGTGGGGGCG CGTTCGTCCT CACTCTCTTC CGCATCGCTG
6061 TCTGCGAGGG CCAGCTGTTG GGGTGAGTAC TCCCTCTCAA AAGCGGGCAT GACTTCTGCG
6121 CTAAGATTGT CAGTTTCCAA AAACGAGGAG GATTTGATAT TCACCTGGCC CGCGGTGATG
6181 CCTTTGAGGG TGGCCGCGTC CATCTGGTCA GAAAAGACAA TCTTTTTGTT GTCAAGCTTG
6241 GTGGCAAACG ACCCGTAGAG GGCGTTGGAC AGCAACTTGG CGATGGAGCG CAGGGTTTGG
6301 TTTTTGTCGC GATCGGCGCG CTCCTTGGCC GCGATGTTTA GCTGCACGTA TTCGCGCGCA
6361 ACGCACCGCC ATTCGGGAAA GACGGTGGTG CGCTCGTCGG GCACTAGGTG CACGCGCCAA
6421 CCGCGGTTGT GCAGGGTGAC AAGGTCAACG CTGGTGGCTA CCTCTCCGCG TAGGCGCTCG
6481 TTGGTCCAGC AGAGGCGGCC GCCCTTGCGC GAGCAGAATG GCGGTAGTGG GTCTAGCTGC
6541 GTCTCGTCCG GGGGGTCTGC GTCCACGGTA AAGACCCCGG GCAGCAGGCG CGCGTCGAAG
6601 TAGTCTATCT TGCATCCTTG CAAGTCTAGC GCCTGCTGCC ATGCGCGGGC GGCAAGCGCG
6661 CGCTCGTATG GGTTGAGTGG GGGACCCCAT GGCATGGGGT GGGTGAGCGC GGAGGCGTAC
6721 ATGCCGCAAA TGTCGTAAAC GTAGAGGGGC TCTCTGAGTA TTCCAAGATA TGTAGGGTAG
6781 CATCTTCCAC CGCGGATGCT GGCGCGCACG TAATCGTATA GTTCGTGCGA GGGAGCGAGG
6841 AGGTCGGGAC CGAGGTTGCT ACGGGCGGGC TGCTCTGCTC GGAAGACTAT CTGCCTGAAG
6901 ATGGCATGTG AGTTGGATGA TATGGTTGGA CGCTGGAAGA CGTTGAAGCT GGCGTCTGTG
6961 AGACCTACCG CGTCACGCAC GAAGGAGGCG TAGGAGTCGC GCAGCTTGTT GACCAGCTCG
7021 GCGGTGACCT GCACGTCTAG GGCGCAGTAG TCCAGGGTTT CCTTGATGAT GTCATACTTA
7081 TCCTGTCCCT TTTTTTTCCA CAGCTCGCGG TTGAGGACAA ACTCTTCGCG GTCTTTCCAG
7141 TACTCTTGGA TCGGAAACCC GTCGGCCTCC GAACGGTAAG AGCCTAGCAT GTAGAACTGG
7201 TTGACGGCCT GGTAGGCGCA GCATCCCTTT TCTACGGGTA GCGCGTATGC CTGCGCGGCC
7261 TTCCGGAGCG AGGTGTGGGT GAGCGCAAAG GTGTCCCTAA CCATGACTTT GAGGTACTGG
7321 TATTTGAAGT CAGTGTCGTC GCATCCGCCC TGCTCCCAGA GCAAAAAGTC CGTGCGCTTT
7381 TTGGAACGCG GGTTTGGCAG GGCGAAGGTG ACATCGTTGA AGAGTATCTT TCCCGCGCGA
7441 GGCATAAAGT TGCGTGTGAT GCGGAAGGGT CCCGGCACCT CGGAACGGTT GTTAATTACC
7501 TGGGCGGCGA GCACGATCTC GTCAAAGCCG TTGATGTTGT GGCCCACAAT GTAAAGTTCC

FIG. 7C

7561 AAGAAGCGCG GGATGCCCTT GATGGAAGGC AATTTTTTAA GTTCCTCGTA GGTGAGCTCT
7621 TCAGGGGAGC TGAGCCCGTG CTCTGAAAGG GCCCAGTCTG CAAGATGAGG GTTGGAAGCG
7681 ACGAATGAGC TCCACAGGTC ACGGGCCATT AGCATTTGCA GGTGGTCGCG AAAGGTCCTA
7741 AACTGGCGAC CTATGGCCAT TTTTTCTGGG GTGATGCAGT AGAAGGTAAG CGGGTCTTGT
7801 TCCCAGCGGT CCCATCCAAG GTCCGCGGCT AGGTCTCGCG CGGCGGTCAC TAGAGGCTCA
7861 TCTCCGCCGA ACTTCATGAC CAGCATGAAG GGCACGAGCT GCTTCCCAAA GGCCCCCATC
7921 CAAGTATAGG TCTCTACATC GTAGGTGACA AAGAGACGCT CGGTGCGAGG ATGCGAGCCG
7981 ATCGGGAAGA ACTGGATCTC CCGCCACCAG TTGGAGGAGT GGCTGTTGAT GTGGTGAAAG
8041 TAGAAGTCCC TGCGACGGGC CGAACACTCG TGCTGGCTTT TGTAAAAACG TGCGCAGTAC
8101 TGGCAGCGGT GCACGGGCTG TACATCCTGC ACGAGGTTGA CCTGACGACC GCGCACAAGG
8161 AAGCAGAGTG GGAATTTGAG CCCCTCGCCT GGCGGGTTTG GCTGGTGGTC TTCTACTTCG
8221 GCTGCTTGTC CTTGACCGTC TGGCTGCTCG AGGGGAGTTA CGGTGGATCG GACCACCACG
8281 CCGCGCGAGC CCAAAGTCCA GATGTCCGCG CGCGGCGGTC GGAGCTTGAT GACAACATCG
8341 CGCAGATGGG AGCTGTCCAT GGTCTGGAGC TCCCGCGGCG TCAGGTCAGG CGGGAGCTCC
8401 TGCAGGTTTA CCTCGCATAG CCGGGTCAGG GCGCGGGCTA GGTCCAGGTG ATACCTGATT
8461 TCCAGGGGCT GGTTGGTGGC GGCGTCGATG GCTTGCAAGA GGCCGCATCC CCGCGGCGCG
8521 ACTACGGTAC CGCGCGGCGG GCGGTGGGCC GCGGGGGTGT CCTTGGATGA TGCATCTAAA
8581 AGCGGTGACG CGGGCGGGCC CCCGGAGGTA GGGGGGGCTC GGGACCCGCC GGGAGAGGGG
8641 GCAGGGGCAC GTCGGCGCCG CGCGCGGGCA GGAGCTGGTG CTGCGCGCGG AGGTTGCTGG
8701 CGAACGCGAC GACGCGGCGG TTGATCTCCT GAATCTGGCG CCTCTGCGTG AAGACGACGG
8761 GCCCGGTGAG CTTGAACCTG AAAGAGAGTT CGACAGAATC AATTTCGGTG TCGTTGACGG
8821 CGGCCTGGCG CAAAATCTCC TGCACGTCTC CTGAGTTGTC TTGATAGGCG ATCTCGGCCA
8881 TGAACTGCTC GATCTCTTCC TCCTGGAGAT CTCCGCGTCC GGCTCGCTCC ACGGTGGCGG
8941 CGAGGTCGTT GGAGATGCGG GCCATGAGCT GCGAGAAGGC GTTGAGGCCT CCCTCGTTCC
9001 AGACGCGGCT GTAGACCACG CCCCCTTCGG CATCGCGGGC GCGCATGACC ACCTGCGCGA
9061 GATTGAGCTC CACGTGCCGG GCGAAGACGG CGTAGTTTCG CAGGCGCTGA AAGAGGTAGT
9121 TGAGGGTGGT GGCGGTGTGT TCTGCCACGA AGAAGTACAT AACCCAGCGC CGCAACGTGG
9181 ATTCGTTGAT ATCCCCCAAG GCCTCAAGGC GCTCCATGGC CTCGTAGAAG TCCACGGCGA
9241 AGTTGAAAAA CTGGGAGTTG CGCGCCGACA CGGTTAACTC CTCCTCCAGA AGACGGATGA
9301 GCTCGGCGAC AGTGTCGCGC ACCTCGCGCT CAAAGGCTAC AGGGGCCTCT TCTTCTTCTT
9361 CAATCTCCTC TTCCATAAGG GCCTCCCCTT CTTCTTCTTC TGGCGGCGGT GGGGGAGGGG
9421 GGACACGGCG GCGACGACGG CGCACCGGGA GGCGGTCGAC AAAGCGCTCG ATCATCTCCC
9481 CGCGGCGACG GCGCATGGTC TCGGTGACGG CGCGGCCGTT CTCGCGGGGG CGCAGTTGGA
9541 AGACGCCGCC CGTCATGTCC CGGTTATGGG TTGGCGGGGG GCTGCCGTGC GGCAGGGATA
9601 CGGCGCTAAC GATGCATCTC AACAATTGTT GTGTAGGTAC TCCGCCACCG AGGGACCTGA
9661 GCGAGTCCGC ATCGACCGGA TCGGAAAACC TCTCGAGAAA GGCGTCTAAC CAGTCACAGT
9721 CGCAAGGTAG GCTGAGCACC GTGGCGGGCG GCAGCGGGCG GCGGTCGGGG TTGTTTCTGG
9781 CGGAGGTGCT GCTGATGATG TAATTAAAGT AGGCGGTCTT GAGACGGCGG ATGGTCGACA
9841 GAAGCACCAT GTCCTTGGGT CCGGCCTGCT GAATGCGCAG GCGGTCGGCC ATGCCCCAGG
9901 CTTCGTTTTG ACATCGGCGC AGGTCTTTGT AGTAGTCTTG CATGAGCCTT TCTACCGGCA
9961 CTTCTTCTTC TCCTTCCTCT TGTCCTGCAT CTCTTGCATC TATCGCTGCG GCGGCGGCGG
10021 AGTTTGGCCG TAGGTGGCGC CCTCTTCCTC CCATGCGTGT GACCCCGAAG CCCCTCATCG

FIG. 7D

10081 GCTGAAGCAG GGCCAGGTCG GCGACAACGC GCTCGGCTAA TATGGCCTGC TGCACCTGCG
10141 TGAGGGTAGA CTGGAAGTCG TCCATGTCCA CAAAGCGGTG GTATGCGCCC GTGTTGATGG
10201 TGTAAGTGCA GTTGGCCATA ACGGACCAGT TAACGGTCTG GTGACCCGGC TGCGAGAGCT
10261 CGGTGTACCT GAGACGCGAG TAAGCCCTTG AGTCAAAGAC GTAGTCGTTG CAAGTCCGCA
10321 CCAGGTACTG GTATCCCACC AAAAAGTGCG GCGGCGGCTG GCGGTAGAGG GGCCAGCGTA
10381 GGGTGGCCGG GGCTCCGGGG GCGAGGTCTT CCAACATAAG GCGATGATAT CCGTAGATGT
10441 ACCTGGACAT CCAGGTGATG CCGGCGGCGG TGGTGGAGGC GCGCGGAAAG TCACGGACGC
10501 GGTTCCAGAT GTTGCGCAGC GGCAAAAAGT GCTCCATGGT CGGGACGCTC TGGCCGGTCA
10561 GGCGCGCGCA GTCGTTGACG CTCTAGACCG TGCAAAAGGA GAGCCTGTAA GCGGGCACTC
10621 TTCCGTGGTC TGGTGGATAA ATTCGCAAGG GTATCATGGC GGACGACCGG GGTTCGAACC
10681 CCGGATCCGG CCGTCCGCCG TGATCCATGC GGTTACCGCC CGCGTGTCGA ACCCAGGTGT
10741 GCGACGTCAG ACAACGGGGG AGCGCTCCTT TTGGCTTCCT TCCAGGCGCG GCGGATGCTG
10801 CGCTAGCTTT TTTGGCCACT GGCCGCGCGC GGCGTAAGCG GTTAGGCTGG AAAGCGAAAG
10861 CATTAAGTGG CTCGCTCCCT GTAGCCGGAG GGTTATTTTC CAAGGGTTGA GTCGCGGGAC
10921 CCCCGGTTCG AGTCTCGGGC CGGCCGGACT GCGGCGAACG GGGGTTTGCC TCCCCGTCAT
10981 GCAAGACCCC GCTTGCAAAT TCCTCCGGAA ACAGGGACGA GCCCCTTTTT TGCTTTTCCC
11041 AGATGCATCC GGTGCTGCGG CAGATGCGCC CCCCTCCTCA GCAGCGGCAA GAGCAAGAGC
11101 AGCGGCAGAC ATGCAGGGCA CCCTCCCCTT CTCCTACCGC GTCAGGAGGG GCAACATCCG
11161 CGGCTGACGC GGCGGCAGAT GGTGATTACG AACCCCCGCG GCGCCGGACC CGGCACTACT
11221 TGGACTTGGA GGAGGGCGAG GGCCTGGCGC GGCTAGGAGC GCCCTCTCCT GAGCGACACC
11281 CAAGGGTGCA GCTGAAGCGT GACACGCGCG AGGCGTACGT GCCGCGGCAG AACCTGTTTC
11341 GCGACCGCGA GGGAGAGGAG CCCGAGGAGA TGCGGGATCG AAAGTTCCAT GCAGGGCGCG
11401 AGTTGCGGCA TGGCCTGAAC CGCGAGCGGT TGCTGCGCGA GGAGGACTTT GAGCCCGACG
11461 CGCGGACCGG GATTAGTCCC GCGCGCGCAC ACGTGGCGGC CGCCGACCTG GTAACCGCGT
11521 ACGAGCAGAC GGTGAACCAG GAGATTAACT TTCAAAAAAG CTTTAACAAC CACGTGCGCA
11581 CGCTTGTGGC GCGCGAGGAG GTGGCTATAG GACTGATGCA TCTGTGGGAC TTTGTAAGCG
11641 CGCTGGAGCA AAACCCAAAT AGCAAGCCGC TCATGGCGCA GCTGTTCCTT ATAGTGCAGC
11701 ACAGCAGGGA CAACGAGGCA TTCAGGGATG CGCTGCTAAA CATAGTAGAG CCCGAGGGCC
11761 GCTGGCTGCT CGATTTGATA AACATTCTGC AGAGCATAGT GGTGCAGGAG CGCAGCTTGA
11821 GCCTGGCTGA CAAGGTGGCC GCCATTAACT ATTCCATGCT CAGTCTGGGC AAGTTTTACG
11881 CCCGCAAGAT ATACCATACC CCTTACGTTC CCATAGACAA GGAGGTAAAG ATCGAGGGGT
11941 TCTACATGCG CATGGCGCTG AAGGTGCTTA CCTTGAGCGA CGACCTGGGC GTTTATCGCA
12001 ACGAGCGCAT CCACAAGGCC GTGAGCGTGA GCCGGCGGCG CGAGCTCAGC GACCGCGAGC
12061 TGATGCACAG CCTGCAAAGG GCCCTGGCTG GCACGGGCAG CGGCGATAGA GAGGCCGAGT
12121 CCTACTTTGA CGCGGGCGCT GACCTGCGCT GGGCCCCAAG CCGACGCGCC CTGGAGGCAG
12181 CTGGGGCCGG ACCTGGGCTG GCGGTGGCAC CCGCGCGCGC TGGCAACGTC GGCGGCGTGG
12241 AGGAATATGA CGAGGACGAT GAGTACGAGC CAGAGGACGG CGAGTACTAA GCGGTGATGT
12301 TTCTGATCAG ATGATGCAAG ACGCAACGGA CCCGGCGGTG CGGGCGGCGC TGCAGAGCCA
12361 GCCGTCCGGC CTTAACTCCA CGGACGACTG GCGCCAGGTC ATGGACCGCA TCATGTCGCT
12421 GACTGCGCGC AACCCTGACG CGTTCCGGCA GCAGCCGCAG GCCAACCGGC TCTCCGCAAT
12481 TCTGGAAGCG GTGGTCCCGG CGCGCGCAAA CCCCACGCAC GAGAAGGTGC TGGCGATCGT
12541 AAACGCGCTG GCCGAAAACA GGGCCATCCG GCCCGATGAG GCCGGCCTGG TCTACGACGC

FIG. 7E

12601 GCTGCTTCAG CGCGTGGCTC GTTACAACAG CAGCAACGTG CAGACCAACC TGGACCGGCT
12661 GGTGGGGGAT GTGCGCGAGG CCGTGGCGCA GCGTGAGCGC GCGCAGCAGC AGGGCAACCT
12721 GGGCTCCATG GTTGCACTAA ACGCCTTCCT GAGTACACAG CCCGCCAACG TGCCGCGGGG
12781 ACAGGAGGAC TACACCAACT TTGTGAGCGC ACTGCGGCTA ATGGTGACTG AGACACCGCA
12841 AAGTGAGGTG TATCAGTCCG GGCCAGACTA TTTTTTCCAG ACCAGTAGAC AAGGCCTGCA
12901 GACCGTAAAC CTGAGCCAGG CTTTCAAGAA CTTGCAGGGG CTGTGGGGGG TGCGGGCTCC
12961 CACAGGCGAC CGCGCGACCG TGTCTAGCTT GCTGACGCCC AACTCGCGCC TGTTGCTGCT
13021 GCTAATAGCG CCCTTCACGG ACAGTGGCAG CGTGTCCCGG GACACATACC TAGGTCACTT
13081 GCTGACACTG TACCGCGAGG CCATAGGTCA GGCGCATGTG GACGAGCATA CTTTCCAGGA
13141 GATTACAAGT GTTAGCCGCG CGCTGGGGCA GGAGGACACG GGCAGCCTGG AGGCAACCCT
13201 GAACTACCTG CTGACCAACC GGCGGCAAAA AATCCCCTCG TTGCACAGTT TAAACAGCGA
13261 GGAGGAGCGC ATTTTGCGCT ATGTGCAGCA GAGCGTGAGC CTTAACCTGA TGCGCGACGG
13321 GGTAACGCCC AGCGTGGCGC TGGACATGAC CGCGCGCAAC ATGGAACCGG GCATGTATGC
13381 CTCAAACCGG CCGTTTATCA ATCGCCTAAT GGACTACTTG CATCGCGCGG CCGCCGTGAA
13441 CCCCGAGTAT TTCACCAATG CCATCTTGAA CCCGCACTGG CTACCGCCCC CTGGTTTCTA
13501 CACCGGGGGA TTCGAGGTGC CCGAGGGTAA CGATGGATTC CTCTGGGACG ACATAGACGA
13561 CAGCGTGTTT TCCCCGCAAC CGCAGACCCT GCTAGAGTTG CAACAACGCG AGCAGGCAGA
13621 GGCGGCGCTG CGAAAGGAAA GCTTCCGCAG GCCAAGCAGC TTGTCCGATC TAGGCGCTGC
13681 GGCCCCGCGG TCAGATGCTA GTAGCCCATT TCCAAGCTTG ATAGGGTCTC TTACCAGCAC
13741 TCGCACCACC CGCCCGCGCC TGCTGGGCGA GGAGGAGTAC CTAAACAACT CGCTGCTGCA
13801 GCCGCAGCGC GAAAAGAACC TGCCTCCGGC GTTTCCCAAC AACGGGATAG AGAGCCTAGT
13861 GGACAAGATG AGTAGATGGA AGACGTATGC GCAGGAGCAC AGGGATGTGC CCGGCCCGCG
13921 CCCGCCCACC CGTCGTCAAA GGCACGACCG TCAGCGGGGT CTGGTGTGGG AGGACGATGA
13981 CTCGGCAGAC GACAGCAGCG TCTTGGATTT GGGAGGGAGT GGCAACCCGT TTGCACACCT
14041 TCGCCCCAGG CTGGGGAGAA TGTTTTAAAA AAGCATGAT GCAAAATAAA AAACTCACCA
14101 AGGCCATGGC ACCGAGCGTT GGTTTTCTTG TATTCCCCTT AGTATGCGGC GCGCGGCGAT
14161 GTATGAGGAA GGTCCTCCTC CCTCCTACGA GAGCGTGGTG AGCGCGGCGC CAGTGGCGGC
14221 GGCGCTGGGT TCACCCTTCG ATGCTCCCCT GGACCCGCCG TTCGTGCCTC CGCGGTACCT
14281 GCGGCCTACC GGGGGGAGAA ACAGCATCCG TTACTCTGAG TTGGCACCCC TATTCGACAC
14341 CACCCGTGTG TACCTTGTGG ACAACAAGTC AACGGATGTG GCATCCCTGA ACTACCAGAA
14401 CGACCACAGC AACTTTCTAA CCACGGTCAT TCAAAACAAT GACTACAGCC CGGGGGAGGC
14461 AAGCACACAG ACCATCAATC TTGACGACCG GTCGCACTGG GGCGGCGACC TGAAAACCAT
14521 CCTGCATACC AACATGCCAA ATGTGAACGA GTTCATGTTT ACCAATAAGT TTAAGGCGCG
14581 GGTGATGGTG TCGCGCTCGC TTACTAAGGA CAAACAGGTG GAGCTGAAAT ACGAGTGGGT
14641 GGAGTTCACG CTGCCCGAGG GCAACTACTC CGAGACCATG ACCATAGACC TTATGAACAA
14701 CGCGATCGTG GAGCACTACT TGAAAGTGGG CAGGCAGAAC GGGGTTCTGG AAAGCGACAT
14761 CGGGGTAAAG TTTGACACCC GCAACTTCAG ACTGGGGTTT GACCCAGTCA CTGGTCTTGT
14821 CATGCCTGGG GTATATACAA ACGAAGCCTT CCATCCAGAC ATCATTTTGC TGCCAGGATG
14881 CGGGGTGGAC TTCACCCACA GCCGCCTGAG CAACTTGTTG GGCATCCGCA AGCGGCAACC
14941 CTTCCAGGAG GGCTTTAGGA TCACCTACGA TGACCTGGAG GGTGGTAACA TTCCCGCACT
15001 GTTGGATGTG GACGCCTACC AGGCAAGCTT GAAAGATGAC ACCGAACAGG GCGGGGGTGG
15061 CGCAGGCGGC GGCAACAACA GTGGCAGCGG CGCGGAAGAG AACTCCAACG CGGCAGCTGC

FIG. 7F

15121 GGCAATGCAG CCGGTGGAGG ACATGAACGA TCATGCCATT CGCGGCGACA CCTTTGCCAC
15181 ACGGGCGGAG GAGAAGCGCG CTGAGGCCGA GGCAGCGGCC GAAGCTGCCG CCCCCGCTGC
15241 GGAGGCTGCA CAACCCGAGG TCGAGAAGCC TCAGAAGAAA CCGGTGATTA AACCCCTGAC
15301 AGAGGACAGC AAGAAACGCA GTTACAACCT AATAAGCAAT GACAGCACCT TCACCCAGTA
15361 CCGCAGCTGG TACCTTGCAT ACAACTACGG CGACCCTCAG GCCGGGATCC GCTCATGGAC
15421 CCTGCTTTGC ACTCCTGACG TAACCTGCGG CTCGGAGCAG GTATACTGGT CGTTGCCCGA
15481 CATGATGCAA GACCCCGTGA CCTTCCGCTC CACGCGCCAG ATCAGCAACT TTCCGGTGGT
15541 GGGCGCCGAG CTGTTGCCCG TGCACTCCAA GAGCTTCTAC AACGACCAGG CCGTCTACTC
15601 CCAGCTCATC CGCCAGTTTA CCTCTCTGAC CCACGTGTTC AATCGCTTTC CCGAGAACCA
15661 GATTTTGGCG CGCCCGCCAG CCCCCACCAT CACCACCGTC AGTGAAAACG TTCCTGCTCT
15721 CACAGATCAC GGGACGCTAC CGCTGCGCAA CAGCATCGGA GGAGTCCAGC GAGTGACCAT
15781 TACTGACGCC AGACGCCGCA CCTGCCCCTA CGTTTACAAG GCCCTGGGCA TAGTCTCGCC
15841 GCGCGTCCTA TCGAGCCGCA CTTTTTGAGC AAGCATGTCC ATCCTTATAT CGCCCAGCAA
15901 TAACACAGGC TGGGGCCTGC GCTTCCCAAG CAAGATGTTT GGCGGGGCCA AGAAGCGCTC
15961 CGACCAACAC CCAGTGCGCG TGCGCGGGCA CTACCGCGCG CCCTGGGGCG CGCACAAACG
16021 CGGCCGCACT GGGCGCACCA CCGTCGATGA CGCCATCGAC GCGGTGGTGG AGGAGGCGCG
16081 CAACTACACG CCCACGCCGC CGCCAGTGTC CACCGTGGAC GCGGCCATTC AGACCGTGGT
16141 GCGCGGAGCC CGGCGCTACG CTAAAATGAA GAGACGGCGG AGGCGCGTAG CACGTCGCCA
16201 CCGCCGCCGA CCCGGCACTG CCGCCCAACG CGCGGCGGCG GCCCTGCTTA ACCGCGCACG
16261 TCGCACCGGC CGACGGGCGG CCATGCGAGC CGCTCGAAGG CTGGCCGCGG GTATTGTCAC
16321 TGTGCCCCCC AGGTCCAGGC GACGAGCGGC CGCCGCAGCA GCCGCGGCCA TTAGTGCTAT
16381 GACTCAGGGT CGCAGGGGCA ACGTGTACTG GGTGCGCGAC TCGGTTAGCG GCCTGCGCGT
16441 GCCCGTGCGC ACCCGCCCCC CGCGCAACTA GATTGCAATA AAAAACTACT TAGACTCGTA
16501 CTGTTGTATG TATCCAGCGG CGGCGGCGCG CATCGAAGCT ATGTCCAAGC GCAAAATCAA
16561 AGAAGAGATG CTCCAGGTCA TCGCGCCGGA GATCTATGGC CCCCCGAAGA AGGAAGAGCA
16621 GGATTACAAG CCCCGAAAGC TAAAGCGGGT CAAAAAGAAA AAGAAAGATG ATGATGATGA
16681 TGAACTTGAC GACGAGGTGG AACTGTTGCA CGCGACCGCG CCCAGGCGAC GGGTACAGTG
16741 GAAAGGTCGA CGCGTAAGAC GTGTTTTGCG ACCCGGCACC ACCGTAGTCT TTACGCCCGG
16801 TGAGCGCTCC ACCCGCACCT ACAAGCGCGT GTATGATGAG GTGTACGGCG ACGAGGACCT
16861 GCTTGAGCAG GCCAACGAGC GCCTCGGGGA GTTTGCCTAC GGAAAGCGGC ATAAGGACAT
16921 GCTGGCGTTG CCGCTGGACG AGGGCAACCC AACACCTAGC CTAAAGCCCG TGACACTGCA
16981 GCAGGTGCTG CCCGCGCTTG CACCGTCCGA AGAAAAGCGC GGCCTAAAGC GCGAGTCTGG
17041 TGACTTGGCA CCCACCGTGC AGCTGATGGT ACCCAAGCGT CAGCGACTGG AAGATGTCTT
17101 GGAAAAAATG ACCGTGGAGC CTGGGCTGGA GCCCGAGGTC CGCGTGCGGC CAATCAAGCA
17161 GGTGGCACCG GGACTGGGCG TGCAGACCGT GGACGTTCAG ATACCCACCA CCAGTAGCAC
17221 TAGTATTGCC ACTGCCACAG AGGGCATGGA GACACAAACG TCCCCGGTTG CCTCGGCGGT
17281 GGCAGATGCC GCGGTGCAGG CGGCCGCTGC GGCCGCGTCC AAGACCTCTA CGGAGGTGCA
17341 AACGGACCCG TGGATGTTTC GTGTTTCAGC CCCCCGGCGT CCGCGCCGTT CAAGGAAGTA
17401 CGGCGCCGCC AGCGCGCTAC TGCCCGAATA TGCCCTACAT CCTTCCATCG CGCCTACCCC
17461 CGGCTATCGT GGCTACACCT ACCGCCCCAG AAGACGAGCA ACTACCCGAC GCCGAACCAC
17521 CACTGGAACC CGCCGCCGCC GTCGCCGTCG CCAGCCCGTG CTGGCCCCGA TTTCCGTGCG
17581 CAGGGTGGCT CGCGAAGGAG GCAGGACCCT GGTGCTGCCA ACAGCGCGCT ACCACCCCAG

FIG. 7G

17641 CATCGTTTAA AAGCCGGTCT TTGTGGTTCT TGCAGATATG GCCCTCACCT GCCGCCTCCG
17701 TTTCCCGGTG CCGGGATTCC GAGGAAGAAT GCACCGTAGG AGGGGCATGG CCGGCCACGG
17761 CCTGACGGGC GGCATGCGTC GTGCGCACCA CCGGCGGCGG CGCGCGTCGC ACCGTCGCAT
17821 GCGCGGCGGT ATCCTGCCCC TCCTTATTCC ACTGATCGCC GCGGCGATTG GCGCCGTGCC
17881 CGGAATTGCA TCCGTGGCCT TGCAGGCGCA GAGACACTGA TTAAAAACAA GTTACATGTG
17941 GAAAAATCAA AATAAAAGTC TGGACTCTCA CGCTCGCTTG GTCCTGTAAC TATTTTGTAG
18001 AATGGAAGAC ATCAACTTTG CGTCACTGGC CCCGCGACAC GGCTCGCGCC CGTTCATGGG
18061 AAACTGGCAA GATATCGGCA CCAGCAATAT GAGCGGTGGC GCCTTCAGCT GGGGCTCGCT
18121 GTGGAGCGGC ATTAAAAATT TCGGTTCCGC CGTTAAGAAC TATGGCAGCA AAGCCTGGAA
18181 CAGCAGCACA GGCCAGATGC TGAGGGACAA GTTGAAAGAG CAAAATTTCC AACAAAAGGT
18241 GGTAGATGGC CTGGCCTCTG GCATTAGCGG GGTGGTGGAC CTGGCCAACC AGGCAGTGCA
18301 AAATAAGATT AACAGTAAGC TTGATCCCCG CCCTCCCGTA GAGGAGCCTC CACCGGCCGT
18361 GGAGACAGTG TCTCCAGAGG GGCGTGGCGA AAAGCGTCCG CGACCCGACA GGGAAGAAAC
18421 TCTGGTGACG CAAATAGACG AGCCTCCCTC GTACGAGGAG GCACTAAAGC AAGGCCTGCC
18481 CACCACCCGT CCCATCGCGC CCATGGCTAC CGGAGTGCTG GGCCAGCACA CACCCGTAAC
18541 GCTGGACCTG CCTCCCCCCG CCGACACCCA GCAGAAACCT GTGCTGCCAG GCCCGTCCGC
18601 CGTTGTTGTA ACCCGTCCTA GCCGCGCGTC CCTGCGCCGC GCCGCCAGCG GTCCGCGATC
18661 GTTGCGGCCC GTAGCCAGTG GCAACTGGCA AAGCACACTG AACAGCATCG TGGGTTTGGG
18721 GGTGCAATCC CTGAAGCGCC GACGATGCTT CTGATAGCTA ACGTGTCGTA TGTGTGTCAT
18781 GTATGCGTCC ATGTCGCCGC CAGAGGAGCT GCTGAGCCGC CGCGCGCCCG CTTTCCAAGA
18841 TGGCTACCCC TTCGATGATG CCGCAGTGGT CTTACATGCA CATCTCGGGC CAGGACGCCT
18901 CGGAGTACCT GAGCCCCGGG CTGGTGCAGT TCGCCCGCGC CACCGAGACG TACTTCAGCC
18961 TGAATAACAA GTTTAGAAAC CCCACGGTGG CGCCTACGCA CGACGTGACC ACAGACCGGT
19021 CTCAGCGTTT GACGCTGCGG TTCATCCCCG TGGACCGCGA GGATACTGCG TACTCGTACA
19081 AGGCGCGGTT CACCCTAGCT GTGGGTGATA ACCGTGTGCT AGACATGGCT TCCACGTACT
19141 TTGACATCCG CGGCGTGCTG GACAGGGGCC CTACTTTTAA GCCCTACTCT GGCACTGCCT
19201 ACAACGCACT GGCCCCCAAG GGTGCCCCCA ACTCGTGCGA GTGGGAACAA AATGAAACTG
19261 CACAAGTGGA TGCTCAAGAA CTTGACGAAG AGGAGAATGA AGCCAATGAA GCTCAGGCGC
19321 GAGAACAGGA ACAAGCTAAG AAAACCCATG TATATGCCCA GGCTCCACTG TCCGGAATAA
19381 AAATAACTAA AGAAGGTCTA CAAATAGGAA CTGCCGACGC CACAGTAGCA GGTGCCGGCA
19441 AAGAAATTTT CGCAGACAAA ACTTTTCAAC CTGAACCACA AGTAGGAGAA TCTCAATGGA
19501 ACGAAGCGGA TGCCACAGCA GCTGGTGGAA GGGTTCTTAA AAAGACAACT CCCATGAAAC
19561 CCTGCTATGG CTCATACGCT AGACCCACCA ATTCCAACGG CGGACAGGGC GTTATGGTTG
19621 AACAAAATGG TAAATTGGAA AGTCAAGTCG AAATGCAATT TTTTTCCACA TCCACAAATG
19681 CCACAAATGA AGTTAACAAT ATACAACCAA CAGTTGTATT GTACAGCGAA GATGTAAACA
19741 TGGAAACTCC AGATACTCAT CTTTCTTATA AACCTAAAAT GGGGGATAAA AATGCCAAAG
19801 TCATGCTTGG ACAACAAGCA ATGCCAAACA GACCAAATTA CATTGCTTTT AGAGACAATT
19861 TTATTGGTCT CATGTATTAC AACAGCACAG GTAACATGGG TGTCCTTGCT GGTCAGGCAT
19921 CGCAGTTGAA CGCTGTTGTA GATTTGCAAG ACAGAAACAC AGAGCTGTCC TACCAGCTTT
19981 TGCTTGATTC AATTGGCGAC AGAACAAGAT ACTTTTCAAT GTGGAATCAA GCTGTTGACA
20041 GCTATGATCC AGATGTCAGA ATTATTGAGA ACCATGGAAC TGAGGATGAG TTGCCAAATT
20101 ATTGCTTTCC TCTTGGTGGA ATTGGGATTA CTGACACTTT TCAAGCTGTT AAAACAACTG

FIG. 7H

20161 CTGCTAACGG GGACCAAGGC AATACTACCT GGCAAAAAGA TTCAACATTT GCAGAACGCA
20221 ATGAAATAGG GGTGGGAAAT AACTTTGCCA TGGAAATTAA CCTGAATGCC AACCTATGGA
20281 GAAATTTCCT TTACTCCAAT ATTGCGCTGT ACCTGCCAGA CAAGCTAAAA TACAACCCCA
20341 CCAATGTGGA AATATCTGAC AACCCCAACA CCTACGACTA CATGAACAAG CGAGTGGTGG
20401 CTCCTGGGCT TGTAGACTGC TACATTAACC TTGGGGCGCG CTGGTCTCTG GACTACATGG
20461 ACAACGTTAA TCCCTTTAAC CACCACCGCA ATGCGGGCCT GCGTTACCGC TCCATGTTGT
20521 TGGGAAACGG CCGCTACGTG CCCTTTCACA TTCAGGTGCC CCAAAAGTTT TTTGCCATTA
20581 AAAACCTCCT CCTCCTGCCA GGCTCATACA CATATGAATG GAACTTCAGG AAGGATGTTA
20641 ACATGGTTCT GCAGAGCTCT CTGGGAAACG ACCTTAGAGT TGACGGGGCT AGCATTAAGT
20701 TTGACAGCAT TTGTCTTTAC GCCACCTTCT TCCCCATGGC CCACAACACG GCCTCCACGC
20761 TGGAAGCCAT GCTCAGAAAT GACACCAACG ACCAGTCCTT TAATGACTAC CTTTCCGCCG
20821 CCAACATGCT ATATCCCATA CCCGCCAACG CCACCAACGT GCCCATCTCC ATCCCATCGC
20881 GCAACTGGGC AGCATTTCGC GGTTGGGCCT TCACACGCTT GAAGACAAAG GAAACCCCTT
20941 CCCTGGGATC AGGCTACGAC CCTTACTACA CCTACTCTGG CTCCATACCA TACCTTGACG
21001 GAACCTTCTA TCTTAATCAC ACCTTTAAGA AGGTGGCCAT TACTTTTGAC TCTTCTGTTA
21061 GCTGGCCGGG CAACGACCGC CTGCTTACTC CCAATGAGTT TGAGATTAAG CGCTCAGTTG
21121 ACGGGGAGGG CTATAACGTA GCTCAGTGCA ACATGACAAA GGACTGGTTC CTAGTGCAGA
21181 TGTTGGCCAA CTACAATATT GGCTACCAGG GCTTCTACAT TCCAGAAAGC TACAAAGACC
21241 GCATGTACTC GTTCTTCAGA AACTTCCAGC CCATGAGCCG GCAAGTGGTG GACGATACTA
21301 AATACAAAGA TTATCAGCAG GTTGGAATTA TCCACCAGCA TAACAACTCA GGCTTCGTAG
21361 GCTACCTCGC TCCCACCATG CGCGAGGGAC AAGCTTACCC CGCTAATGTT CCCTACCCAC
21421 TAATAGGCAA AACCGCGGTT GATAGTATTA CCCAGAAAAA GTTTCTTTGC GACCGCACCC
21481 TGTGGCGCAT CCCCTTCTCC AGTAACTTTA TGTCCATGGG TGCGCTCACA GACCTGGGCC
21541 AAAACCTTCT CTACGCAAAC TCCGCCCACG CGCTAGACAT GACCTTTGAG GTGGATCCCA
21601 TGGACGAGCC CACCCTTCTT TATGTTTTGT TTGAAGTCTT TGACGTGGTC CGTGTGCACC
21661 AGCCGCACCG CGGCGTCATC GAGACCGTGT ACCTGCGCAC GCCCTTCTCG GCCGGCAACG
21721 CCACAACATA AAGAAGCAAG CAACATCAAC AACAGCTGCC GCCATGGGCT CCAGTGAGCA
21781 GGAACTGAAA GCCATTGTCA AAGATCTTGG TTGTGGGCCA TATTTTTTGG GCACCTATGA
21841 CAAGCGCTTC CCAGGCTTTG TTTCCCCACA CAAGCTCGCC TGCGCCATAG TTAACACGGC
21901 CGGTCGCGAG ACTGGGGGCG TACACTGGAT GGCCTTTGCC TGGAACCCGC GCTCAAAAAC
21961 ATGCTACCTC TTTGAGCCCT TTGGCTTTTC TGACCAACGT CTCAAGCAGG TTTACCAGTT
22021 TGAGTACGAG TCACTCCTGC GCCGTAGCGC CATTGCCTCT TCCCCCGACC GCTGTATAAC
22081 GCTGGAAAAG TCCACCCAAA GCGTGCAGGG GCCCAACTCG GCCGCCTGTG GCCTATTCTG
22141 CTGCATGTTT CTCCACGCCT TTGCCAACTG GCCCCAAACT CCCATGGATC ACAACCCCAC
22201 CATGAACCTT ATTACCGGGG TACCCAACTC CATGCTTAAC AGTCCCCAGG TACAGCCCAC
22261 CCTGCGCCGC AACCAGGAAC AGCTCTACAG CTTCCTGGAG CGCCACTCGC CCTACTTCCG
22321 CAGCCACAGT GCGCAAATTA GGAGCGCCAC TTCTTTTTGT CACTTGAAAA ACATGTAAAA
22381 ATAATGTACT AGGAGACACT TTCAATAAAG GCAAATGTTT TTATTTGTAC ACTCTCGGGT
22441 GATTATTTAC CCCCACCCTT GCCGTCTGCG CCGTTTAAAA ATCAAAGGGG TTCTGCCGCG
22501 CATCGCTATG CGCCACTGGC AGGGACACGT TGCGATACTG GTGTTTAGTG CTCCACTTAA
22561 ACTCAGGCAC AACCATCCGC GGCAGCTCGG TGAAGTTTTC ACTCCACAGG CTGCGCACCA
22621 TCACCAACGC GTTTAGCAGG TCGGGCGCCG ATATCTTGAA GTCGCAGTTG GGGCCTCCGC

FIG. 7I

22681 CCTGCGCGCG CGAGTTGCGA TACACAGGGT TACAGCACTG GAACACTATC AGCGCCGGGT
22741 GGTGCACGCT GGCCAGCACG CTCTTGTCGG AGATCAGATC CGCGTCCAGG TCCTCCGCGT
22801 TGCTCAGGGC GAACGGAGTC AACTTTGGTA GCTGCCTTCC CAAAAAGGGT GCATGCCCAG
22861 GCTTTGAGTT GCACTCGCAC CGTAGTGGCA TCAGAAGGTG ACCGTGCCCA GTCTGGGCGT
22921 TAGGATACAG CGCCTGCATG AAAGCCTTGA TCTGCTTAAA AGCCACCTGA GCCTTTGCGC
22981 CTTCAGAGAA GAACATGCCG CAAGACTTGC CGGAAAACTG ATTGGCCGGA CAGGCCGCGT
23041 CATGCACGCA GCACCTTGCG TCGGTGTTGG AGATCTGCAC CACATTTCGG CCCCACCGGT
23101 TCTTCACGAT CTTGGCCTTG CTAGACTGCT CCTTCAGCGC GCGCTGCCCG TTTTCGCTCG
23161 TCACATCCAT TTCAATCACG TGCTCCTTAT TTATCATAAT GCTCCCGTGT AGACACTTAA
23221 GCTCGCCTTC GATCTCAGCG CAGCGGTGCA GCCACAACGC GCAGCCCGTG GGCTCGTGGT
23281 GCTTGTAGGT TACCTCTGCA AACGACTGCA GGTACGCCTG CAGGAATCGC CCCATCATCG
23341 TCACAAAGGT CTTGTTGCTG GTGAAGGTCA GCTGCAACCC GCGGTGCTCC TCGTTTAGCC
23401 AGGTCTTGCA TACGGCCGCC AGAGCTTCCA CTTGGTCAGG CAGTAGCTTG AAGTTTGCCT
23461 TTAGATCGTT ATCCACGTGG TACTTGTCCA TCAACGCGCG CGCAGCCTCC ATGCCCTTCT
23521 CCCACGCAGA CACGATCGGC AGGCTCAGCG GGTTTATCAC CGTGCTTTCA CTTTCCGCTT
23581 CACTGGACTC TTCCTTTTCC TCTTGCATCC GCATACCCCG CGCCACTGGG TCGTCTTCAT
23641 TCAGCCGCCG CACCGTGCGC TTACCTCCCT TGCCGTGCTT GATTAGCACC GGTGGGTTGC
23701 TGAAACCCAC CATTTGTAGC GCCACATCTT CTCTTTCTTC CTCGCTGTCC ACGATCACCT
23761 CTGGGGATGG CGGGCGCTCG GGCTTGGGAG AGGGGCGCTT CTTTTTCTTT TTGGACGCAA
23821 TGGCCAAATC CGCCGTCGAG GTCGATGGCC GCGGGCTGGG TGTGCGCGGC ACCAGCGCAT
23881 CTTGTGACGA GTCTTCTTCG TCCTCGGACT CGAGACGCCG CCTCAGCCGC TTTTTTGGGG
23941 GCGCGCGGGG AGGCGGCGGC GACGGCGACG GGGACGAGAC GTCCTCCATG GTTGGTGGAC
24001 GTCGCGCCGC ACCGCGTCCG CGCTCGGGGG TGGTTTCGCG CTGCTCCTCT TCCCGACTGG
24061 CCATTTCCTT CTCCTATAGG CAGAAAAAGA TCATGGAGTC AGTCGAGAAG GAGGACAGCC
24121 TAACCGCCCC CTTTGAGTTC GCCACCACCG CCTCCACCGA TGCCGCCAAC GCGCCTACCA
24181 CCTTCCCCGT CGAGGCACCC CCGCTTGAGG AGGAGGAAGT GATTATCGAG CAGGACCCAG
24241 GTTTTGTAAG CGAAGACGAC GAAGATCGCT CAGTACCAAC AGAGGATAAA AAGCAAGACC
24301 AGGACGACGC AGAGGCAAAC GAGGAACAAG TCGGGCGGGG GGACCAAAGG CATGGCGACT
24361 ACCTAGATGT GGGAGACGAC GTGCTGTTGA AGCATCTGCA GCGCCAGTGC GCCATTATCT
24421 GCGACGCGTT GCAAGAGCGC AGCGATGTGC CCCTCGCCAT AGCGGATGTC AGCCTTGCCT
24481 ACGAACGCCA CCTGTTCTCA CCGCGCGTAC CCCCCAAACG CCAAGAAAAC GGCACATGCG
24541 AGCCCAACCC GCGCCTCAAC TTCTACCCCG TATTTGCCGT GCCAGAGGTG CTTGCCACCT
24601 ATCACATCTT TTTCCAAAAC TGCAAGATAC CCCTATCCTG CCGTGCCAAC CGCAGCCGAG
24661 CGGACAAGCA GCTGGCCTTG CGGCAGGGCG CTGTCATACC TGATATCGCC TCGCTCGACG
24721 AAGTGCCAAA AATCTTTGAG GGTCTTGGAC GCGACGAGAA GCGCGCGGCA AACGCTCTGC
24781 AACAAGAAAA CAGCGAAAAT GAAAGTCACT GTGGAGTGCT GGTGGAACTT GAGGGTGACA
24841 ACGCGCGCCT AGCCGTGCTG AAACGCAGCA TCGAGGTCAC CCACTTTGCC TACCCGGCAC
24901 TTAACCTACC CCCCAAGGTT ATGAGCACAG TCATGAGCGA GCTGATCGTG CGCCGTGCAC
24961 GACCCCTGGA GAGGGATGCA AACTTGCAAG AACAAACCGA GGAGGGCCTA CCCGCAGTTG
25021 GCGATGAGCA GCTGGCGCGC TGGCTTGAGA CGCGCGAGCC TGCCGACTTG GAGGAGCGAC
25081 GCAAGCTAAT GATGGCCGCA GTGCTTGTTA CCGTGGAGCT TGAGTGCATG CAGCGGTTCT
25141 TTGCTGACCC GGAGATGCAG CGCAAGCTAG AGGAAACGTT GCACTACACC TTTCGCCAGG

FIG. 7J

25201 GCTACGTGCG CCAGGCCTGC AAAATTTCCA ACGTGGAGCT CTGCAACCTG GTCTCCTACC
25261 TTGGAATTTT GCACGAAAAC CGCCTTGGGC AAAACGTGCT TCATTCCACG CTCAAGGGCG
25321 AGGCGCGCCG CGACTACGTC CGCGACTGCG TTTACTTATT TCTGTGCTAC ACCTGGCAAA
25381 CGGCCATGGG CGTGTGGCAG CAGTGCCTGG AGGAGCGCAA CCTGAAGGAG CTGCAGAAGC
25441 TGCTAAAGCA AAACTTGAAG GACCTATGGA CGGCCTTCAA CGAGCGCTCC GTGGCCGCGC
25501 ACCTGGCGGA CATTATCTTC CCCGAACGCC TGCTTAAAAC CCTGCAACAG GGTCTGCCAG
25561 ACTTCACCAG TCAAAGCATG TTGCAAAACT TTAGGAACTT TATCCTAGAG CGTTCAGGAA
25621 TTCTGCCCGC CACCTGCTGT GCGCTTCCTA GCGACTTTGT GCCCATTAAG TACCGTGAAT
25681 GCCCTCCGCC GCTTTGGGGT CACTGCTACC TTCTGCAGCT AGCCAACTAC CTTGCCTACC
25741 ACTCCGACAT CATGGAAGAC GTGAGCGGTG ACGGCCTACT GGAGTGTCAC TGTCGCTGCA
25801 ACCTATGCAC CCCGCACCGC TCCCTGGTCT GCAATTCACA ACTGCTTAGC GAAAGTCAAA
25861 TTATCGGTAC CTTTGAGCTG CAGGGTCCCT CGCCTGACGA AAAGTCCGCG GCTCCGGGGT
25921 TGAAACTCAC TCCGGGGCTG TGGACGTCGG CTTACCTTCG CAAATTTGTA CCTGAGGACT
25981 ACCACGCCCA CGAGATTAGG TTCTACGAAG ACCAATCCCG CCCGCCAAAT GCGGAGCTTA
26041 CCGCCTGCGT CATTACCCAG GGCCACATCC TTGGCCAATT GCAAGCCATT AACAAAGCCC
26101 GCCAAGAGTT TCTGCTACGA AAGGGACGGG GGGTTTACTT GGACCCCCAG TCCGGCGAGG
26161 AGCTCAACCC AATCCCCCCG CCGCCGCAGC CCTATCAGCA GCCGCGGGCC CTTGCTTCCC
26221 AGGATGGCAC CCAAAAAGAA GCTGCAGCTG CCGCCGCCGC CACCCACGGA CGAGGAGGAA
26281 TACTGGGACA GTCAGGCAGA GGAGGTTTTG GACGAGGAGG AGGAGATGAT GGAAGACTGG
26341 GACAGCCTAG ACGAGGAAGC TTCCGAGGCC GAAGAGGTGT CAGACGAAAC ACCGTCACCC
26401 TCGGTCGCAT TCCCCTCGCC GGCGCCCCAG AAATCGGCAA CCGTTCCCAG CATTGCTACA
26461 ACCTCCGCTC CTCAGGCGCC GCCGGCACTG CCCGTTCGCC GACCCAACCG TAGATGGGAC
26521 ACCACTGGAA CCAGGGCCGG TAAGTCTAAG CAGCCGCCGC CGTTAGCCCA AGAGCAACAA
26581 CAGCGCCAAG GCTACCGCTC GTGGCGCGTG CACAAGAACG CCATAGTTGC TTGCTTGCAA
26641 GACTGTGGGG GCAACATCTC CTTCGCCCGC CGCTTTCTTC TCTACCATCA CGGCGTGGCC
26701 TTCCCCCGTA ACATCCTGCA TTACTACCGT CATCTCTACA GCCCCTACTG CACCGGCGGC
26761 AGCGGCAGCA ACAGCAGCGG CCACGCAGAA GCAAAGGCGA CCGGATAGCA AGACTCTGAC
26821 AAAGCCCAAG AAATCCACAG CGGCGGCAGC AGCAGGAGGA GGAGCACTGC GTCTGGCGCC
26881 CAACGAACCC GTATCGACCC GCGAGCTTAG AAACAGGATT TTTCCCACTC TGTATGCTAT
26941 ATTTCAACAG AGCAGGGGCC AAGAACAAGA GCTGAAAATA AAAAACAGGT CTCTGCGCTC
27001 CCTCACCCGC AGCTGCCTGT ATCACAAAAG CGAAGATCAG CTTCGGCGCA CGCTGGAAGA
27061 CGCGGAGGCT CTCTTCAGCA AATACTGCGC GCTGACTCTT AAGGACTAGT TTCGCGCCCT
27121 TTCTCAAATT TAAGCGCGAA AACTACGTCA TCTCCAGCGG CCACACCCGG CGCCAGCACC
27181 TGTCGTCAGC GCCATTATGA GCAAGGAAAT TCCCACGCCC TACATGTGGA GTTACCAGCC
27241 ACAAATGGGA CTTGCGGCTG GAGCTGCCCA AGACTACTCA ACCCGAATAA ACTACATGAG
27301 CGCGGGACCC CACATGATAT CCCGGGTCAA CGGAATCCGC GCCCACCGAA ACCGAATTCT
27361 CCTCGAACAG GCGGCTATTA CCACCACACC TCGTAATAAC CTTAATCCCC GTAGTTGGCC
27421 CGCTGCCCTG GTGTACCAGG AAAGTCCCGC TCCCACCACT GTGGTACTTC CCAGAGACGC
27481 CCAGGCCGAA GTTCAGATGA CTAACTCAGG GGCGCAGCTT GCGGGCGGCT TTCGTCACAG
27541 GGTGCGGTCG CCCGGGCAGG GTATAACTCA CCTGAAAATC AGAGGGCGAG GTATTCAGCT
27601 CAACGACGAG TCGGTGAGCT CCTCTCTTGG TCTCCGTCCG GACGGGACAT TTCAGATCGG
27661 CGGCGCTGGC CGCTCTTCAT TTACGCCCCG TCAGGCGATC CTAACTCTGC AGACCTCGTC

FIG. 7K

27721 CTCGGAGCCG CGCTCCGGAG GCATTGGAAC TCTACAATTT ATTGAGGAGT TCGTGCCTTC
27781 GGTTTACTTC AACCCCTTTT CTGGACCTCC CGGCCACTAC CCGGACCAGT TTATTCCCAA
27841 CTTTGACGCG GTAAAAGACT CGGCGGACGG CTACGACTGA ATGACCAGTG GAGAGGCAGA
27901 GCAACTGCGC CTGACACACC TCGACCACTG CCGCCGCCAC AAGTGCTTTG CCCGCGGCTC
27961 CGGTGAGTTT TGTTACTTTG AATTGCCCGA AGAGCATATC GAGGGCCCGG CGCACGGCGT
28021 CCGGCTCACC ACCCAGGTAG AGCTTACACG TAGCCTGATT CGGGAGTTTA CCAAGCGCCC
28081 CCTGCTAGTG GAGCGGGAGC GGGGTCCCTG TGTTCTGACC GTGGTTTGCA ACTGTCCTAA
28141 CCCTGGATTA CATCAAGATC TTTGTTGTCA TCTCTGTGCT GAGTATAATA AATACAGAAA
28201 TTAGAATCTA CTGGGGCTCC TGTCGCCATC CTGTGAACGC CACCGTTTTT ACCCACCCAA
28261 AGCAGACCAA AGCAAACCTC ACCTCCGGTT TGCACAAGCG GGCCAATAAG TACCTTACCT
28321 GGTACTTTAA CGGCTCTTCA TTTGTAATTT ACAACAGTTT CCAGCGAGAC GAAGTAAGTT
28381 TGCCACACAA CCTTCTCGGC TTCAACTACA CCGTCAAGAA AAACACCACC ACCACCCTCC
28441 TCACCTGCCG GGAACGTACG AGTGCGTCAC CGGTTGCTGC GCCCACACCT ACAGCCTGAG
28501 CGTAACCAGA CATTACTCCC ATTTTCCCAA AACAGGAGGT GAGCTCAACT CCCGGAACTC
28561 AGGTCAAAAA AGCATTTTGC GGGGTGCTGG GATTTTTTAA TTAAGTATAT GAGCAATTCA
28621 AGTAACTCTA CAAGCTTGTC TAATTTTTCT GGAATTGGGG TCGGGGTTAT CCTTACTCTT
28681 GTAATTCTGT TTATTCTTAT ACTAGCACTT CTGTGCCTTA GGGTTGCCGC CTGCTGCACG
28741 CACGTTTGTA CCTATTGTCA GCTTTTTAAA CGCTGGGGGC GACATCCAAG ATGAGGTACA
28801 TGATTTTAGG CTTGCTCGCC CTTGCGGCAG TCTGCAGCGC TGCCAAAAAG GTTGAGTTTA
28861 AGGAACCAGC TTGCAATGTT ACATTTAAAT CAGAAGCTAA TGAATGCACT ACTCTTATAA
28921 AATGCACCAC AGAACATGAA AAGCTTATTA TTCGCCACAA AGACAAAATT GGCAAGTATG
28981 CTGTATATGC TATTTGGCAG CCAGGTGACA CTAACGACTA TAATGTCACA GTCTTCCAAG
29041 GTGAAAATCG TAAAACTTTT ATGTATAAAT TTCCATTTTA TGAAATGTGC GATATTACCA
29101 TGTACATGAG CAAACAGTAC AAGTTGTGGC CCCCACAAAA GTGTTTAGAG AACACTGGCA
29161 CCTTTTGTTC CACCGCTCTG CTTATTACAG CGCTTGCTTT GGTATGTACC TTACTTTATC
29221 TCAAATACAA AAGCAGACGC AGTTTTATTG ATGAAAAGAA AATGCCTTGA TTTTCCGCTT
29281 GCTTGTATTC CCCTGGACAA TTTACTCTAT GTGGGATATG CGCCAGGCGG GAAAGATTAT
29341 ACCCACAACC TTCAAATCAA ACTTTCCTGG ACGTTAGCGC CTGACTTCTG CCAGCGCCTG
29401 CACTGCAAAT TTGATCAAAC CCAGCTTCAG CTTGCCTGCT CCAGAGATGA CCGGCTCAAC
29461 CATCGCGCCC ACAACGGACT ATCGCAACAC CACTGCTACC GGACTAAAAT CTGCCCTAAA
29521 TTTACCCCAA GTTCATGCCT TTGTCAATGA CTGGGCGAGC TTGGGCATGT GGTGGTTTTC
29581 CATAGCGCTT ATGTTTGTTT GCCTTATTAT TATGTGGCTT ATTTGTTGCC TAAAGCGCAG
29641 ACGCGCCAGA CCCCCCATCT ATAGGCCTAT CATTGTGCTC AACCCACACA ATGAAAAAAT
29701 TCATAGATTG GACGGTCTCA AACCATGTTC TCTTCTTTTA CAGTATGATT AAATGAGACA
29761 TGATTCCTCG AGTCCTTATA TTATTGACCC TTGTTGCGCT TTTCTGTGCG TGCTCTACAT
29821 TGGCTGCGGT CGCTCACATC GAAGTAGATT GCATCCCACC TTTCACAGTT TACCTGCTTT
29881 ACGGATTTGT CACCCTTATC CTCATCTGCA GCCTCGTCAC TGTAGTCATC GCCTTCATTC
29941 AGTTCATTGA CTGGATTTGT GTGCGCATTG CGTACCTTAG GCACCATCCG CAATACAGAG
30001 ACAGGACTAT AGCTGATCTT CTCAGAATTC TTTAATTATG AAACGGATTG TCACTTTTGT
30061 TTTGCTGATT TTCTGCGCCC TACCTGTGCT TTGCTCCCAA ACCTCAGCGC CTCCCAAAAG
30121 ACATATTTCC TGCAGATTCA CTCAAATATG GAACATTCCC AGCTGCTACA ACAAACAGAG
30181 CGATTTGTCA GAAGCCTGGT TATACGCCAT CATCTCTGTC ATGGTTTTTT GCAGTACCAT

FIG. 7L

30241 TTTTGCCCTA GCCATATACC CATACCTTGA CATTGGTTGG AATGCCATAG ATGCCATGAA
30301 CCACCCTACT TTCCCAGCGC CCAATGTCAT ACCACTGCAA CAGGTTATTG CCCCAATCAA
30361 TCAGCCTCGC CCCCCTTCTC CCACCCCCAC TGAGATTAGC TACTTTAATT TGACAGGTGG
30421 AGATGACTGA ATCTCTAGAT CTAGAATTGG ATGGAATTAA CACCGAACAG CGCCTACTAG
30481 AAAGGCGCAA GGCGGCGTCC GAGCGAGAAC GCCTAAAACA AGAAGTTGAA GACATGGTTA
30541 ACCTGCACCA GTGTAAAAGA GGTATCTTTT GTGTGGTCAA GCAGGCCAAA CTTACCTACG
30601 AAAAAACCAC TACCGGCAAC CGCCTTAGCT ACAAGCTACC CACCCAGCGC CAAAAACTGG
30661 TGCTTATGGT GGGAGAAAAA CCTATCACCG TCACCCAGCA CTCGGCAGAA ACAGAAGGCT
30721 GCCTGCACTT CCCCTATCAG GGTCCAGAGG ACCTCTGCAC TCTTATTAAA ACCATGTGTG
30781 GCATTAGAGA TCTTATTCCA TTCAACTAAC AATAAACACA CAATAAATTA CTTACTTAAA
30841 ATCAGTCAGC AAATCTTTGT CCAGCTTATT CAGCATCACC TCCTTTCCCT CCTCCCAACT
30901 CTGGTATTTC AGCAGCCTTT TAGCTGCGAA CTTTCTCCAA AGTCTAAATG GGATGTCAAA
30961 TTCCTCATGT TCTTGTCCCT CCGCACCCAC TATCTTCATA TTGTTGCAGA TGAAACGCGC
31021 CAGACCGTCT GAAGACACCT TCAACCCTGT GTACCCATAT GACACGGAAA CCGGCCCTCC
31081 AACTGTGCCT TTCCTTACCC CTCCCTTTGT GTCGCCAAAT GGGTTCCAAG AAAGTCCCCC
31141 CGGAGTGCTT TCTTTGCGTC TTTCAGAACC TTTGGTTACC TCACACGGCA TGCTTGCGCT
31201 AAAAATGGGC AGCGGCCTGT CCCTGGATCA GGCAGGCAAC CTTACATCAA ATACAATCAC
31261 TGTTTCTCAA CCGCTAAAAA AAACAAAGTC CAATATAACT TTGGAAACAT CCGCGCCCCT
31321 TACAGTCAGC TCAGGCGCCC TAACCATGGC CACAACTTCG CCTTTGGTGG TCTCTGACAA
31381 CACTCTTACC ATGCAATCAC AAGCACCGCT AACCGTGCAA GACTCAAAAC TTAGCATTGC
31441 TACCAAAGAG CCACTTACAG TGTTAGATGG AAAACTGGCC CTGCAGACAT CAGCCCCCCT
31501 CTCTGCCACT GATAACAACG CCCTCACTAT CACTGCCTCA CCTCCTCTTA CTACTGCAAA
31561 TGGTAGTCTG GCTGTTACCA TGGAAAACCC ACTTTACAAC AACAATGGAA AACTTGGGCT
31621 CAAAATTGGC GGTCCTTTGC AAGTGGCCAC CGACTCACAT GCACTAACAC TAGGTACTGG
31681 TCAGGGGGTT GCAGTTCATA ACAATTTGCT ACATACAAAA GTTACAGGCG CAATAGGGTT
31741 TGATACATCT GGCAACATGG AACTTAAAAC TGGAGATGGC CTCTATGTGG ATAGCGCCGG
31801 TCCTAACCAA AAACTACATA TTAATCTAAA TACCACAAAA GGCCTTGCTT TTGACAACAC
31861 CGCAATAACA ATTAACGCTG GAAAAGGGTT GGAATTTGAA ACAGACTCCT CAAACGGAAA
31921 TCCCATAAAA ACAAAAATTG GATCAGGCAT ACAATATAAT ACCAATGGAG CTATGGTTGC
31981 AAAACTTGGA ACAGGCCTCA GTTTTGACAG CTCCGGAGCC ATAACAATGG GCAGCATAAA
32041 CAATGACAGA CTTACTCTTT GGACAACACC AGACCCATCC CCAAATTGCA GAATTGCTTC
32101 AGATAAAGAC TGCAAGCTAA CTCTGGCGCT AACAAAATGT GGCAGTCAAA TTTTGGGCAC
32161 TGTTTCAGCT TTGGCAGTAT CAGGTAATAT GGCCTCCATC AATGGAACTC TAAGCAGTGT
32221 AAACTTGGTT CTTAGATTTG ATGACAACGG AGTGCTTATG TCAAATTCAT CACTGGACAA
32281 ACAGTATTGG AACTTTAGAA ACGGGGACTC CACTAACGGT CAACCATACA CTTATGCTGT
32341 TGGGTTTATG CCAAACCTAA AAGCTTACCC AAAAACTCAA AGTAAAACTG CAAAAAGTAA
32401 TATTGTTAGC CAGGTGTATC TTAATGGTGA CAAGTCTAAA CCATTGCATT TTACTATTAC
32461 GCTAAATGGA ACAGATGAAA CCAACCAAGT AAGCAAATAC TCAATATCAT TCAGTTGGTC
32521 CTGGAACAGT GGACAATACA CTAATGACAA ATTTGCCACC AATTCCTATA CCTTCTCCTA
32581 CATTGCCCAG GAATAAAGAA TCGTGAACCT GTTGCATGTT ATGTTTCAAC GTGTTTATTT
32641 TTCAATTGCA GAAAATTTCA AGTCATTTTT CATTCAGTAG TATAGCCCCA CCACCACATA
32701 GCTTATACTA ATCACCGTAC CTTAATCAAA CTCACAGAAC CCTAGTATTC AACCTGCCAC

FIG. 7M

32761 CTCCCTCCCA ACACACAGAG TACACAGTCC TTTCTCCCCG GCTGGCCTTA AACAGCATCA
32821 TATCATGGGT AACAGACATA TTCTTAGGTG TTATATTCCA CACGGTCTCC TGTCGAGCCA
32881 AACGCTCATC AGTGATGTTA ATAAACTCCC CGGGCAGCTC GCTTAAGTTC ATGTCGCTGT
32941 CCAGCTGCTG AGCCACAGGC TGCTGTCCAA CTTGCGGTTG CTCAACGGGC GGCGAAGGAG
33001 AAGTCCACGC CTACATGGGG GTAGAGTCAT AATCGTGCAT CAGGATAGGG CGGTGGTGCT
33061 GCAGCAGCGC GCGAATAAAC TGCTGCCGCC GCCGCTCCGT CCTGCAGGAA TACAACATGG
33121 CAGTGGTCTC CTCAGCGATG ATTCGCACCG CCCGCAGCAT AAGGCGCCTT GTCCTCCGGG
33181 CACAGCAGCG CACCCTGATC TCACTTAAGT CAGCACAGTA ACTGCAGCAC AGTACCACAA
33241 TATTGTTTAA AATCCCACAG TGCAAGGCGC TGTATCCAAA GCTCATGGCG GGGACCACAG
33301 AACCCACGTG GCCATCATAC CACAAGCGCA GGTAGATTAA GTGGCGACCC CTCATAAACA
33361 CGCTGGACAT AAACATTACC TCTTTTGGCA TGTTGTAATT CACCACCTCC CGGTACCATA
33421 TAAACCTCTG ATTAAACATG GCGCCATCCA CCACCATCCT AAACCAGCTG GCCAAAACCT
33481 GCCCGCCGGC TATGCACTGC AGGGAACCGG GACTGGAACA ATGACAGTGG AGAGCCCAGG
33541 ACTCGTAACC ATGGATCATC ATGCTCGTCA TGATATCAAT GTTGGCACAA CACAGGCACA
33601 CGTGCATACA CTTCCTCAGG ATTACAAGCT CCTCCCGCGT CAGAACCATA TCCCAGGGAA
33661 CAACCCATTC CTGAATCAGC GTAAATCCCA CACTGCAGGG AAGACCTCGC ACGTAACTCA
33721 CGTTGTGCAT TGTCAAAGTG TTACATTCGG GCAGCAGCGG ATGATCCTCC AGTATGGTAG
33781 CGCGTGTCTC TGTCTCAAAA GGAGGTAGGC GATCCCTACT GTACGGAGTG CGCCGAGACA
33841 ACCGAGATCG TGTTGGTCGT AGTGTCATGC CAAATGGAAC GCCGGACGTA GTCATATTTC
33901 CTGAAGCAAA ACCAGGTGCG GGCGTGACAA ACAGATCTGC GTCTCCGGTC TCGTCGCTTA
33961 GCTCGCTCTG TGTAGTAGTT GTAGTATATC CACTCTCTCA AAGCATCCAG GCGCCCCCTG
34021 GCTTCGGGTT CTATGTAAAC TCCTTCATGC GCCGCTGCCC TGATAACATC CACCACCGCA
34081 GAATAAGCCA CACCCAGCCA ACCTACACAT TCGTTCTGCG AGTCACACAC GGGAGGAGCG
34141 GGAAGAGCTG GAAGAACCAT GTTTTTTTTT TTTATTCCAA AAGATTATCC AAAACCTCAA
34201 AATGAAGATC TATTAAGTGA ACGCGCTCCC CTCCGGTGGC GTGGTCAAAC TCTACAGCCA
34261 AAGAACAGAT AATGGCATTT GTAAGATGTT GCACAATGGC TTCCAAAAGG CAAACTGCCC
34321 TCACGTCCAA GTGGACGTAA AGGCTAAACC CTTCAGGGTG AATCTCCTCT ATAAACATTC
34381 CAGCACCTTC AACCATGCCC AAATAATTTT CATCTCGCCA CCTTATCAAT ATGTCTCTAA
34441 GCAAATCCCG AATATTAAGT CCGGCCATTG TAAAAATCTG CTCCAGAGCG CCCTCCACCT
34501 TCAGCCTCAA GCAGCGAATC ATGATTGCAA AAATTCAGGT TCCTCACAGA CCTGTATAAG
34561 ATTCAAAAGC GGAACATTAA CAAAAATACC GCGATCCCGT AGGTCCCTTC GCAGGGCCAG
34621 CTGAACATAA TCGTGCAGGT CTGCACGGAC CAGCGCGGCC ACTTCCCCGC CAGGAACCAT
34681 GACAAAAGAA CCCACACTGA TTATGACACG CATACTCGGA GCTATGCTAA CCAGCGTAGC
34741 CCCGATGTAA GCTTGTTGCA TGGGCGGCGA TATAAAATGC AAGGTACTGC TCAAAAAATC
34801 AGGCAAAGCC TCGCGCAAAA AAGCAAGCAC ATCGTAGTCA TGCTCATGCA GATAAAGGCA
34861 GGTAAGTTCC GGAACCACCA CAGAAAAAGA CACCATTTTT CTCTCAAACA TGTCTGCGGG
34921 TTCCTGCATA AACACAAAAT AAAATAACAA AAAAAAAAAA ACATTTAAAC ATTAGAAGCC
34981 TGTNTTACAA CAGGAAAAAC AACCCTTATA AGCATAAGAC GGACTACGGC CATGCCGGCG
35041 TGACCGTAAA AAAACTGGTC ACCGTGATTA AAAAGCACCA CCGACAGTTC CTCGGTCATG
35101 TCCGGAGTCA TAATGTAAGA CTCGGTAAAC ACATCAGGTT GGTTAACATC GGTCAGTGCT
35161 AAAAAGCGAC CGAAATAGCC CGGGGGAATA CATACCCGCA GGCGTAGAGA CAACATTACA
35221 GCCCCCATAG GAGGTATAAC AAAATTAATA GGAGAGAAAA ACACATAAAC ACCTGAAAAA

FIG. 7N

35281 CCCTCCTGCC TAGGCAAAAT AGCACCCTCC CGCTCCAGAA CAACATACAG CGCTTCCACA
35341 GCGGCAGCCA TAACAGTCAG CCTTACCAGT AAAAAAACCT ATTAAAAAAC ACCACTCGAC
35401 ACGGCACCAG CTCAATCAGT CACAGTGTAA AAAGGGCCAA GTACAGAGCG AGTATATATA
35461 GGACTAAAAA ATGACGTAAC GGTTAAAGTC CACAAAAACC ACCCAGAAAA CCGCACGCGA
35521 ACCTACGCCC AGAAACGAAA GCCAAAAAAC CCACAACTTC CTCAAATCTT CACTTCCGTT
35581 TTCCCACGAT ACGTCACTTC CCATTTTAAA AAAAAACTAC AATTCCCAAT ACATGCAAGT
35641 TACTCCGCCC TAAAACCTAC GTCACCCGCC CCGTTCCCAC GCCCCGCGCC ACGTCACAAA
35701 CTCCACCCCC TCATTATCAT ATTGGCTTCA ATCCAAAATA AGGTATATTA TTGATGATG

FIG. 7O

```
   1 CATCATCAAT AATATACCTT ATTTTGGATT GAAGCCAATA TGATAATGAG GGGGTGGAGT
  61 TTGTGACGTG GCGCGGGGCG TGGGAACGGG GCGGGTGACG TAGTAGTGTG GCGGAAGTGT
 121 GATGTTGCAA GTGTGGCGGA ACACATGTAA GCGACGGATG TGGCAAAAGT GACGTTTTTG
 181 GTGTGCGCCG GTGTACACAG GAAGTGACAA TTTTCGCGCG GTTTTAGGCG GATGTTGTAG
 241 TAAATTTGGG CGTAACCGAG TAAGATTTGG CCATTTTCGC GGGAAAACTG AATAAGAGGA
 301 AGTGAAATCT GAATAATTTT GTGTTACTCA TAGCGCGTAA TATTTGTCTA GGGCCGCGGG
 361 GACTTTGACC GTTTACGTGG AGACTCGCCC AGGTGTTTTT CTCAGGTGTT TTCCGCGTTC
 421 CGGGTCAAAG TTGGCGTTTT ATTATTATAG TCAGCTGACG TGTAGTGTAT TTATACCCGG
 481 TGAGTTCCTC AAGAGGCCAC TCTTGAGTGC CAGCGAGTAG AGTTTTCTCC TCCGAGCCGC
 541 TCCGACACCG GGACTGAAAA TGAGACATAT TATCTGCCAC GGAGGTGTTA TTACCGAAGA
 601 AATGGCCGCC AGTCTTTTGG ACCAGCTGAT CGAAGAGGTA CTGGCTGATA ATCTTCCACC
 661 TCCTAGCCAT TTTGAACCAC CTACCCTTCA CGAACTGTAT GATTTAGACG TGACGGCCCC
 721 CGAAGATCCC AACGAGGAGG CGGTTTCGCA GATTTTTCCC GACTCTGTAA TGTTGGCGGT
 781 GCAGGAAGGG ATTGACTTAC TCACTTTTCC GCCGGCGCCC GGTTCTCCGG AGCCGCCTCA
 841 CCTTTCCCGG CAGCCCGAGC AGCCGGAGCA GAGAGCCTTG GGTCCGGTTT CTATGCCAAA
 901 CCTTGTACCG GAGGTGATCG ATCTTACCTG CCACGAGGCT GGCTTTCCAC CCAGTGACGA
 961 CGAGGATGAA GAGGGTGAGG AGTTTGTGTT AGATTATGTG GAGCACCCCG GGCACGGTTG
1021 CAGGTCTTGT CATTATCACC GGAGGAATAC GGGGGACCCA GATATTATGT GTTCGCTTTG
1081 CTATATGAGG ACCTGTGGCA TGTTTGTCTA CAGTAAGTGA AAATTATGGG CAGTGGGTGA
1141 TAGAGTGGTG GGTTTGGTGT GGTAATTTTT TTTTTAATTT TTACAGTTTT GTGGTTTAAA
1201 GAATTTTGTA TTGTGATTTT TTTAAAAGGT CCTGTGTCTG AACCTGAGCC TGAGCCCGAG
1261 CCAGAACCGG AGCCTGCAAG ACCTACCCGC CGTCCTAAAA TGGCGCCTGC TATCCTGAGA
1321 CGCCCGACAT CACCTGTGTC TAGAGAATGC AATAGTAGTA CGGATAGCTG TGACTCCGGT
1381 CCTTCTAACA CACCTCCTGA GATACACCCG GTGGTCCCGC TGTGCCCCAT TAAACCAGTT
1441 GCCGTGAGAG TTGGTGGGCG TCGCCAGGCT GTGGAATGTA TCGAGGACTT GCTTAACGAG
1501 CCTGGGCAAC CTTTGGACTT GAGCTGTAAA CGCCCCAGGC CATAAGGTGT AAACCTGTGA
1561 TTGCGTGTGT GGTTAACGCC TTTGTTTGCT GAATGAGTTG ATGTAAGTTT AATAAAGGGT
1621 GAGATAATGT TTAACTTGCA TGGCGTGTTA AATGGGGCGG GGCTTAAAGG GTATATAATG
1681 CGCCGTGGGC TAATCTTGGT TACATCTGAC CTCATGGAGG CTTGGGAGTG TTTGGAAGAT
1741 TTTTCTGCTG TGCGTAACTT GCTGGAACAG AGCTCTAACA GTACCTCTTG GTTTTGGAGG
1801 TTTCTGTGGG GCTCATCCCA GGCAAAGTTA GTCTGCAGAA TTAAGGAGGA TTACAAGTGG
1861 GAATTTGAAG AGCTTTTGAA ATCCTGTGGT GAGCTGTTTG ATTCTTTGAA TCTGGGTCAC
1921 CAGGCGCTTT TCCAAGAGAA GGTCATCAAG ACTTTGGATT TTTCCACACC GGGGCGCGCT
1981 GCGGCTGCTG TTGCTTTTTT GAGTTTTATA AAGGATAAAT GGAGCGAAGA AACCCATCTG
2041 AGCGGGGGGT ACCTGCTGGA TTTTCTGGCC ATGCATCTGT GGAGAGCGGT TGTGAGACAC
2101 AAGAATCGCC TGCTACTGTT GTCTTCCGTC CGCCCGGCGA TAATACCGAC GGAGGAGCAG
2161 CAGCAGCAGC AGGAGGAAGC CAGGCGGCGG CGGCAGGAGC AGAGCCCATG GAACCCGAGA
2221 GCCGGCCTGG ACCCTCGGGA ATGAATGTTG TACAGGTGGC TGAACTGTAT CCAGAACTGA
2281 GACGCATTTT GACAATTACA GAGGATGGGC AGGGGCTAAA GGGGGTAAAG AGGGAGCGGG
2341 GGGCTTGTGA GGCTACAGAG GAGGCTAGGA ATCTAGCTTT TAGCTTAATG ACCAGACACC
2401 GTCCTGAGTG TATTACTTTT CAACAGATCA AGGATAATTG CGCTAATGAG CTTGATCTGC
2461 TGGCGCAGAA GTATTCCATA GAGCAGCTGA CCACTTACTG GCTGCAGCCA GGGGATGATT
2521 TTGAGGAGGC TATTAGGGTA TATGCAAAGG TGGCACTTAG GCCAGATTGC AAGTACAAGA
2581 TCAGCAAACT TGTAAATATC AGGAATTGTT GCTACATTTC TGGGAACGGG GCCGAGGTGG
2641 AGATAGATAC GGAGGATAGG GTGGCCTTTA GATGTAGCAT GATAAATATG TGGCCGGGGG
2701 TGCTTGGCAT GGACGGGGTG GTTATTATGA ATGTAAGGTT TACTGGCCCC AATTTTAGCG
2761 GTACGGTTTT CCTGGCCAAT ACCAACCTTA TCCTACACGG TGTAAGCTTC TATGGGTTTA
2821 ACAATACCTG TGTGGAAGCC TGGACCGATG TAAGGGTTCG GGGCTGTGCC TTTTACTGCT
2881 GCTGGAAGGG GGTGGTGTGT CGCCCCAAAA GCAGGGCTTC AATTAAGAAA TGCCTCTTTG
2941 AAAGGTGTAC CTTGGGTATC CTGTCTGAGG GTAACTCCAG GGTGCGCCAC AATGTGGCCT
3001 CCGACTGTGG TTGCTTCATG CTAGTGAAAA GCGTGGCTGT GATTAAGCAT AACATGGTAT
3061 GTGGCAACTG CGAGGACAGG GCCTCTCAGA TGCTGACCTG CTCGGACGGC AACTGTCACC
3121 TGCTGAAGAC CATTCACGTA GCCAGCCACT CTCGCAAGGC CTGGCCAGTG TTTGAGCATA
3181 ACATACTGAC CCGCTGTTCC TTGCATTTGG GTAACAGGAG GGGGGTGTTC CTACCTTACC
3241 AATGCAATTT GAGTCACACT AAGATATTGC TTGAGCCCGA GAGCATGTCC AAGGTGAACC
```

FIG. 8A

```
3301 TGAACGGGGT GTTTGACATG ACCATGAAGA TCTGGAAGGT GCTGAGGTAC GATGAGACCC
3361 GCACCAGGTG CAGACCCTGC GAGTGTGGCG GTAAACATAT TAGGAACCAG CCTGTGATGC
3421 TGGATGTGAC CGAGGAGCTG AGGCCCGATC ACTTGGTGCT GGCCTGCACC CGCGCTGAGT
3481 TTGGCTCTAG CGATGAAGAT ACAGATTGAG GTACTGAAAT GTGTGGGCGT GGCTTAAGGG
3541 TGGGAAAGAA TATATAAGGT GGGGGTCTTA TGTAGTTTTG TATCTGTTTT GCAGCAGCCG
3601 CCGCCGCCAT GAGCACCAAC TCGTTTGATG GAAGCATTGT GAGCTCATAT TTGACAACGC
3661 GCATGCCCCC ATGGGCCGGG GTGCGTCAGA ATGTGATGGG CTCCAGCATT GATGGTCGCC
3721 CCGTCCTGCC CGCAAACTCT ACTACCTTGA CCTACGAGAC CGTGTCTGGA ACGCCGTTGG
3781 AGACTGCAGC CTCCGCCGCC GCTTCAGCCG CTGCAGCCAC CGCCCGCGGG ATTGTGACTG
3841 ACTTTGCTTT CCTGAGCCCG CTTGCAAGCA GTGCAGCTTC CCGTTCATCC GCCCGCGATG
3901 ACAAGTTGAC GGCTCTTTTG GCACAATTGG ATTCTTTGAC CCGGGAACTT AATGTCGTTT
3961 CTCAGCAGCT GTTGGATCTG CGCCAGCAGG TTTCTGCCCT GAAGGCTTCC TCCCCTCCCA
4021 ATGCGGTTTA AAACATAAAT AAAAAACCAG ACTCTGTTTG GATTTGGATC AAGCAAGTGT
4081 CTTGCTGTCT TTATTTAGGG GTTTTGCGCG CGCGGTAGGC CCGGGACCAG CGGTCTCGGT
4141 CGTTGAGGGT CCTGTGTATT TTTTCCAGGA CGTGGTAAAG GTGACTCTGG ATGTTCAGAT
4201 ACATGGGCAT AAGCCCGTCT CTGGGGTGGA GGTAGCACCA CTGCAGAGCT TCATGCTGCG
4261 GGGTGGTGTT GTAGATGATC CAGTCGTAGC AGGAGCGCTG GGCGTGGTGC CTAAAAATGT
4321 CTTTCAGTAG CAAGCTGATT GCCAGGGGCA GGCCCTTGGT GTAAGTGTTT ACAAAGCGGT
4381 TAAGCTGGGA TGGGTGCATA CGTGGGGATA TGAGATGCAT CTTGGACTGT ATTTTTAGGT
4441 TGGCTATGTT CCCAGCCATA TCCCTCCGGG GATTCATGTT GTGCAGAACC ACCAGCACAG
4501 TGTATCCGGT GCACTTGGGA AATTTGTCAT GTAGCTTAGA AGGAAATGCG TGGAAGAACT
4561 TGGAGACGCC CTTGTGACCT CCAAGATTTT CCATGCATTC GTCCATAATG ATGGCAATGG
4621 GCCCACGGGC GGCGGCCTGG GCGAAGATAT TTCTGGGATC ACTAACGTCA TAGTTGTGTT
4681 CCAGGATGAG ATCGTCATAG GCCATTTTTA CAAAGCGCGG GCGGAGGGTG CCAGACTGCG
4741 GTATAATGGT TCCATCCGGC CCAGGGGCGT AGTTACCCTC ACAGATTTGC ATTTCCCACG
4801 CTTTGAGTTC AGATGGGGGG ATCATGTCTA CCTGCGGGGC GATGAAGAAA ACGGTTTCCG
4861 GGGTAGGGGA GATCAGCTGG GAAGAAAGCA GGTTCCTGAG CAGCTGCGAC TTACCGCAGC
4921 CGGTGGGCCC GTAAATCACA CCTATTACCG GGTGCAACTG GTAGTTAAGA GAGCTGCAGC
4981 TGCCGTCATC CCTGAGCAGG GGGGCCACTT CGTTAAGCAT GTCCCTGACT CGCATGTTTT
5041 CCCTGACCAA ATCCGCCAGA AGGCGCTCGC CGCCCAGCGA TAGCAGTTCT TGCAAGGAAG
5101 CAAAGTTTTT CAACGGTTTG AGACCGTCCG CCGTAGGCAT GCTTTTGAGC GTTTGACCAA
5161 GCAGTTCCAG GCGGTCCCAC AGCTCGGTCA CCTGCTCTAC GGCATCTCGA TCCAGCATAT
5221 CTCCTCGTTT CGCGGGTTGG GGCGGCTTTC GCTGTACGGC AGTAGTCGGT GCTCGTCCAG
5281 ACGGGCCAGG GTCATGTCTT TCCACGGGCG CAGGGTCCTC GTCAGCGTAG TCTGGGTCAC
5341 GGTGAAGGGG TGCGCTCCGG GCTGCGCGCT GGCCAGGGTG CGCTTGAGGC TGGTCCTGCT
5401 GGTGCTGAAG CGCTGCCGGT CTTCGCCCTG CGCGTCGGCC AGGTAGCATT TGACCATGGT
5461 GTCATAGTCC AGCCCCTCCG CGGCGTGGCC CTTGGCGCGC AGCTTGCCCT TGGAGGAGGC
5521 GCCGCACGAG GGGCAGTGCA GACTTTTGAG GGCGTAGAGC TTGGGCGCGA GAAATACCGA
5581 TTCCGGGGAG TAGGCATCCG CGCCGCAGGC CCCGCAGACG GTCTCGCATT CCACGAGCCA
5641 GGTGAGCTCT GGCCGTTCGG GGTCAAAAAC CAGGTTTCCC CCATGCTTTT TGATGCGTTT
5701 CTTACCTCTG GTTTCCATGA GCCGGTGTCC ACGCTCGGTG ACGAAAAGGC TGTCCGTGTC
5761 CCCGTATACA GACTTGAGAG GCCTGTCCTC GAGCGGTGTT CCGCGGTCCT CCTCGTATAG
5821 AAACTCGGAC CACTCTGAGA CAAAGGCTCG CGTCCAGGCC AGCACGAAGG AGGCTAAGTG
5881 GGAGGGGTAG CGGTCGTTGT CCACTAGGGG GTCCACTCGC TCCAGGGTGT GAAGACACAT
5941 GTCGCCCTCT TCGGCATCAA GGAAGGTGAT TGGTTTGTAG GTGTAGGCCA CGTGACCGGG
6001 TGTTCCTGAA GGGGGGCTAT AAAAGGGGGT GGGGGCGCGT TCGTCCTCAC TCTCTTCCGC
6061 ATCGCTGTCT GCGAGGGCCA GCTGTTGGGG TGAGTACTCC CTCTGAAAAG CGGGCATGAC
6121 TTCTGCGCTA AGATTGTCAG TTTCCAAAAA CGAGGAGGAT TTGATATTCA CCTGGCCCGC
6181 GGTGATGCCT TTGAGGGTGG CCGCATCCAT CTGGTCAGAA AAGACAATCT TTTTGTTGTC
6241 AAGCTTGGTG GCAAACGACC CGTAGAGGGC GTTGGACAGC AACTTGGCGA TGGAGCGCAG
6301 GGTTTGGTTT TTGTCGCGAT CGGCGCGCTC CTTGGCCGCG ATGTTTAGCT GCACGTATTC
6361 GCGCGCAACG CACCGCCATT CGGGAAAGAC GGTGGTGCGC TCGTCGGGCA CCAGGTGCAC
6421 GCGCCAACCG CGGTTGTGCA GGGTGACAAG GTCAACGCTG GTGGCTACCT CTCCGCGTAG
6481 GCGCTCGTTG GTCCAGCAGA GGCGGCCGCC CTTGCGCGAG CAGAATGGCG GTAGGGGGTC
6541 TAGCTGCGTC TCGTCCGGGG GGTCTGCGTC CACGGTAAAG ACCCCGGGCA GCAGGCGCGC
```

FIG. 8B

```
6601 GTCGAAGTAG TCTATCTTGC ATCCTTGCAA GTCTAGCGCC TGCTGCCATG CGCGGGCGGC
6661 AAGCGCGCGC TCGTATGGGT TGAGTGGGGG ACCCCATGGC ATGGGGTGGG TGAGCGCGGA
6721 GGCGTACATG CCGCAAATGT CGTAAACGTA GAGGGGCTCT CTGAGTATTC CAAGATATGT
6781 AGGGTAGCAT CTTCCACCGC GGATGCTGGC GCGCACGTAA TCGTATAGTT CGTGCGAGGG
6841 AGCGAGGAGG TCGGGACCGA GGTTGCTACG GGCGGGCTGC TCTGCTCGGA AGACTATCTG
6901 CCTGAAGATG GCATGTGAGT TGGATGATAT GGTTGGACGC TGGAAGACGT TGAAGCTGGC
6961 GTCTGTGAGA CCTACCGCGT CACGCACGAA GGAGGCGTAG GAGTCGCGCA GCTTGTTGAC
7021 CAGCTCGGCG GTGACCTGCA CGTCTAGGGC GCAGTAGTCC AGGGTTTCCT TGATGATGTC
7081 ATACTTATCC TGTCCCTTTT TTTTCCACAG CTCGCGGTTG AGGACAAACT CTTCGCGGTC
7141 TTTCCAGTAC TCTTGGATCG GAAACCCGTC GGCCTCCGAA CGGTAAGAGC CTAGCATGTA
7201 GAACTGGTTG ACGGCCTGGT AGGCGCAGCA TCCCTTTTCT ACGGGTAGCG CGTATGCCTG
7261 CGCGGCCTTC CGGAGCGAGG TGTGGGTGAG CGCAAAGGTG TCCCTGACCA TGACTTTGAG
7321 GTACTGGTAT TTGAAGTCAG TGTCGTCGCA TCCGCCCTGC TCCCAGAGCA AAAAGTCCGT
7381 GCGCTTTTTG GAACGCGGAT TTGGCAGGGC GAAGGTGACA TCGTTGAAGA GTATCTTTCC
7441 CGCGCGAGGC ATAAAGTTGC GTGTGATGCG GAAGGGTCCC GGCACCTCGG AACGGTTGTT
7501 AATTACCTGG GCGGCGAGCA CGATCTCGTC AAAGCCGTTG ATGTTGTGGC CCACAATGTA
7561 AAGTTCCAAG AAGCGCGGGA TGCCCTTGAT GGAAGGCAAT TTTTTAAGTT CCTCGTAGGT
7621 GAGCTCTTCA GGGGAGCTGA GCCCGTGCTC TGAAAGGGCC CAGTCTGCAA GATGAGGGTT
7681 GGAAGCGACG AATGAGCTCC ACAGGTCACG GGCCATTAGC ATTTGCAGGT GGTCGCGAAA
7741 GGTCCTAAAC TGGCGACCTA TGGCCATTTT TTCTGGGGTG ATGCAGTAGA AGGTAAGCGG
7801 GTCTTGTTCC CAGCGGTCCC ATCCAAGGTT CGCGGCTAGG TCTCGCGCGG CAGTCACTAG
7861 AGGCTCATCT CCGCCGAACT TCATGACCAG CATGAAGGGC ACGAGCTGCT TCCCAAAGGC
7921 CCCCATCCAA GTATAGGTCT CTACATCGTA GGTGACAAAG AGACGCTCGG TGCGAGGATG
7981 CGAGCCGATC GGGAAGAACT GGATCTCCCG CCACCAATTG GAGGAGTGGC TATTGATGTG
8041 GTGAAAGTAG AAGTCCCTGC GACGGGCCGA ACACTCGTGC TGGCTTTTGT AAAAACGTGC
8101 GCAGTACTGG CAGCGGTGCA CGGGCTGTAC ATCCTGCACG AGGTTGACCT GACGACCGCG
8161 CACAAGGAAG CAGAGTGGGA ATTTGAGCCC CTCGCCTGGC GGGTTTGGCT GGTGGTCTTC
8221 TACTTCGGCT GCTTGTCCTT GACCGTCTGG CTGCTCGAGG GGAGTTACGG TGGATCGGAC
8281 CACCACGCCG CGCGAGCCCA AAGTCCAGAT GTCCGCGCGC GGCGGTCGGA GCTTGATGAC
8341 AACATCGCGC AGATGGGAGC TGTCCATGGT CTGGAGCTCC CGCGGCGTCA GGTCAGGCGG
8401 GAGCTCCTGC AGGTTTACCT CGCATAGACG GGTCAGGGCG CGGGCTAGAT CCAGGTGATA
8461 CCTAATTTCC AGGGGCTGGT TGGTGGCGGC GTCGATGGCT TGCAAGAGGC CGCATCCCCG
8521 CGGCGCGACT ACGGTACCGC GCGGCGGGCG GTGGGCCGCG GGGGTGTCCT TGGATGATGC
8581 ATCTAAAAGC GGTGACGCGG GCGAGCCCCC GGAGGTAGGG GGGGCTCCGG ACCCGCCGGG
8641 AGAGGGGGCA GGGGCACGTC GGCGCCGCGC GCGGGCAGGA GCTGGTGCTG CGCGCGTAGG
8701 TTGCTGGCGA ACGCGACGAC GCGGCGGTTG ATCTCCTGAA TCTGGCGCCT CTGCGTGAAG
8761 ACGACGGGCC CGGTGAGCTT GAGCCTGAAA GAGAGTTCGA CAGAATCAAT TTCGGTGTCG
8821 TTGACGGCGG CCTGGCGCAA AATCTCCTGC ACGTCTCCTG AGTTGTCTTG ATAGGCGATC
8881 TCGGCCATGA ACTGCTCGAT CTCTTCCTCC TGGAGATCTC CGCGTCCGGC TCGCTCCACG
8941 GTGGCGGCGA GGTCGTTGGA AATGCGGGCC ATGAGCTGCG AGAAGGCGTT GAGGCCTCCC
9001 TCGTTCCAGA CGCGGCTGTA GACCACGCCC CCTTCGGCAT CGCGGGCGCG CATGACCACC
9061 TGCGCGAGAT TGAGCTCCAC GTGCCGGGCG AAGACGGCGT AGTTTCGCAG GCGCTGAAAG
9121 AGGTAGTTGA GGGTGGTGGC GGTGTGTTCT GCCACGAAGA AGTACATAAC CCAGCGTCGC
9181 AACGTGGATT CGTTGATATC CCCCAAGGCC TCAAGGCGCT CCATGGCCTC GTAGAAGTCC
9241 ACGGCGAAGT TGAAAAACTG GGAGTTGCGC GCCGACACGG TTAACTCCTC CTCCAGAAGA
9301 CGGATGAGCT CGGCGACAGT GTCGCGCACC TCGCGCTCAA AGGCTACAGG GGCCTCTTCT
9361 TCTTCTTCAA TCTCCTCTTC CATAAGGGCC TCCCCTTCTT CTTCTTCTGG CGGCGGTGGG
9421 GGAGGGGGGA CACGGCGGCG ACGACGGCGC ACCGGGAGGC GGTCGACAAA GCGCTCGATC
9481 ATCTCCCCGC GGCGACGGCG CATGGTCTCG GTGACGGCGC GGCCGTTCTC GCGGGGGCGC
9541 AGTTGGAAGA CGCCGCCCGT CATGTCCCGG TTATGGGTTG GCGGGGGGCT GCCATGCGGC
9601 AGGGATACGG CGCTAACGAT GCATCTCAAC AATTGTTGTG TAGGTACTCC GCCGCCGAGG
9661 GACCTGAGCG AGTCCGCATC GACCGGATCG GAAAACCTCT CGAGAAAGGC GTCTAACCAG
9721 TCACAGTCGC AAGGTAGGCT GAGCACCGTG GCGGGCGGCA GCGGGCGGCG GTCGGGGTTG
9781 TTTCTGGCGG AGGTGCTGCT GATGATGTAA TTAAAGTAGG CGGTCTTGAG ACGGCGGATG
9841 GTCGACAGAA GCACCATGTC CTTGGGTCCG GCCTGCTGAA TGCGCAGGCG GTCGGCCATG
```

FIG. 8C

```
 9901 CCCCAGGCTT CGTTTTGACA TCGGCGCAGG TCTTTGTAGT AGTCTTGCAT GAGCCTTTCT
 9961 ACCGGCACTT CTTCTTCTCC TTCCTCTTGT CCTGCATCTC TTGCATCTAT CGCTGCGGCG
10021 GCGGCGGAGT TTGGCCGTAG GTGGCGCCCT CTTCCTCCCA TGCGTGTGAC CCCGAAGCCC
10081 CTCATCGGCT GAAGCAGGGC TAGGTCGGCG ACAACGCGCT CGGCTAATAT GGCCTGCTGC
10141 ACCTGCGTGA GGGTAGACTG GAAGTCATCC ATGTCCACAA AGCGGTGGTA TGCGCCCGTG
10201 TTGATGGTGT AAGTGCAGTT GGCCATAACG GACCAGTTAA CGGTCTGGTG ACCCGGCTGC
10261 GAGAGCTCGG TGTACCTGAG ACGCGAGTAA GCCCTCGAGT CAAATACGTA GTCGTTGCAA
10321 GTCCGCACCA GGTACTGGTA TCCCACCAAA AAGTGCGGCG GCGGCTGGCG GTAGAGGGGC
10381 CAGCGTAGGG TGGCCGGGGC TCCGGGGGCG AGATCTTCCA ACATAAGGCG ATGATATCCG
10441 TAGATGTACC TGGACATCCA GGTGATGCCG GCGGCGGTGG TGGAGGCGCG CGGAAAGTCG
10501 CGGACGCGGT TCCAGATGTT GCGCAGCGGC AAAAAGTGCT CCATGGTCGG GACGCTCTGG
10561 CCGGTCAGGC GCGCGCAATC GTTGACGCTC TAGACCGTGC AAAAGGAGAG CCTGTAAGCG
10621 GGCACTCTTC CGTGGTCTGG TGGATAAATT CGCAAGGGTA TCATGGCGGA CGACCGGGGT
10681 TCGAGCCCCG TATCCGGCCG TCCGCCGTGA TCCATGCGGT TACCGCCCGC GTGTCGAACC
10741 CAGGTGTGCG ACGTCAGACA ACGGGGGAGT GCTCCTTTTG GCTTCCTTCC AGGCGCGGCG
10801 GCTGCTGCGC TAGCTTTTTT GGCCACTGGC CGCGCGCAGC GTAAGCGGTT AGGCTGGAAA
10861 GCGAAAGCAT TAAGTGGCTC GCTCCCTGTA GCCGGAGGGT TATTTTCCAA GGGTTGAGTC
10921 GCGGGACCCC CGGTTCGAGT CTCGGACCGG CCGGACTGCG GCGAACGGGG GTTTGCCTCC
10981 CCGTCATGCA AGACCCCGCT TGCAAATTCC TCCGGAAACA GGGACGAGCC CCTTTTTTGC
11041 TTTTCCCAGA TGCATCCGGT GCTGCGGCAG ATGCGCCCCC CTCCTCAGCA GCGGCAAGAG
11101 CAAGAGCAGC GGCAGACATG CAGGGCACCC TCCCCTCCTC CTACCGCGTC AGGAGGGGCG
11161 ACATCCGCGG TTGACGCGGC AGCAGATGGT GATTACGAAC CCCCGCGGCG CCGGGCCCGG
11221 CACTACCTGG ACTTGGAGGA GGGCGAGGGC CTGGCGCGGC TAGGAGCGCC CTCTCCTGAG
11281 CGGTACCCAA GGGTGCAGCT GAAGCGTGAT ACGCGTGAGG CGTACGTGCC GCGGCAGAAC
11341 CTGTTTCGCG ACCGCGAGGG AGAGGAGCCC GAGGAGATGC GGGATCGAAA GTTCCACGCA
11401 GGGCGCGAGC TGCGGCATGG CCTGAATCGC GAGCGGTTGC TGCGCGAGGA GGACTTTGAG
11461 CCCGACGCGC GAACCGGGAT TAGTCCCGCG CGCGCACACG TGGCGGCCGC CGACCTGGTA
11521 ACCGCATACG AGCAGACGGT GAACCAGGAG ATTAACTTTC AAAAAAGCTT TAACAACCAC
11581 GTGCGTACGC TTGTGGCGCG CGAGGAGGTG GCTATAGGAC TGATGCATCT GTGGGACTTT
11641 GTAAGCGCGC TGGAGCAAAA CCCAAATAGC AAGCCGCTCA TGGCGCAGCT GTTCCTTATA
11701 GTGCAGCACA GCAGGGACAA CGAGGCATTC AGGGATGCGC TGCTAAACAT AGTAGAGCCC
11761 GAGGGCCGCT GGCTGCTCGA TTTGATAAAC ATCCTGCAGA GCATAGTGGT GCAGGAGCGC
11821 AGCTTGAGCC TGGCTGACAA GGTGGCCGCC ATCAACTATT CCATGCTTAG CCTGGGCAAG
11881 TTTTACGCCC GCAAGATATA CCATACCCCT TACGTTCCCA TAGACAAGGA GGTAAAGATC
11941 GAGGGGTTCT ACATGCGCAT GGCGCTGAAG GTGCTTACCT TGAGCGACGA CCTGGGCGTT
12001 TATCGCAACG AGCGCATCCA CAAGGCCGTG AGCGTGAGCC GGCGGCGCGA GCTCAGCGAC
12061 CGCGAGCTGA TGCACAGCCT GCAAAGGGCC CTGGCTGGCA CGGGCAGCGG CGATAGAGAG
12121 GCCGAGTCCT ACTTTGACGC GGGCGCTGAC CTGCGCTGGG CCCCAAGCCG ACGCGCCCTG
12181 GAGGCAGCTG GGGCCGGACC TGGGCTGGCG GTGGCACCCG CGCGCGCTGG CAACGTCGGC
12241 GGCGTGGAGG AATATGACGA GGACGATGAG TACGAGCCAG AGGACGGCGA GTACTAAGCG
12301 GTGATGTTTC TGATCAGATG ATGCAAGACG CAACGGACCC GGCGGTGCGG GCGGCGCTGC
12361 AGAGCCAGCC GTCCGGCCTT AACTCCACGG ACGACTGGCG CCAGGTCATG GACCGCATCA
12421 TGTCGCTGAC TGCGCGCAAT CCTGACGCGT TCCGGCAGCA GCCGCAGGCC AACCGGCTCT
12481 CCGCAATTCT GGAAGCGGTG GTCCCGGCGC GCGCAAACCC CACGCACGAG AAGGTGCTGG
12541 CGATCGTAAA CGCGCTGGCC GAAAACAGGG CCATCCGGCC CGACGAGGCC GGCCTGGTCT
12601 ACGACGCGCT GCTTCAGCGC GTGGCTCGTT ACAACAGCGG CAACGTGCAG ACCAACCTGG
12661 ACCGGCTGGT GGGGGATGTG CGCGAGGCCG TGGCGCAGCG TGAGCGCGCG CAGCAGCAGG
12721 GCAACCTGGG CTCCATGGTT GCACTAAACG CCTTCCTGAG TACACAGCCC GCCAACGTGC
12781 CGCGGGGACA GGAGGACTAC ACCAACTTTG TGAGCGCACT GCGGCTAATG GTGACTGAGA
12841 CACCGCAAAG TGAGGTGTAC CAGTCTGGGC CAGACTATTT TTTCCAGACC AGTAGACAAG
12901 GCCTGCAGAC CGTAAACCTG AGCCAGGCTT TCAAAAACTT GCAGGGGCTG TGGGGGGTGC
12961 GGGCTCCCAC AGGCGACCGC GCGACCGTGT CTAGCTTGCT GACGCCCAAC TCGCGCCTGT
13021 TGCTGCTGCT AATAGCGCCC TTCACGGACA GTGGCAGCGT GTCCCGGGAC ACATACCTAG
13081 GTCACTTGCT GACACTGTAC CGCGAGGCCA TAGGTCAGGC GCATGTGGAC GAGCATACTT
13141 TCCAGGAGAT TACAAGTGTC AGCCGCGCGC TGGGGCAGGA GGACACGGGC AGCCTGGAGG
```

FIG. 8D

13201 CAACCCTAAA CTACCTGCTG ACCAACCGGC GGCAGAAGAT CCCCTCGTTG CACAGTTTAA
13261 ACAGCGAGGA GGAGCGCATT TTGCGCTACG TGCAGCAGAG CGTGAGCCTT AACCTGATGC
13321 GCGACGGGGT AACGCCCAGC GTGGCGCTGG ACATGACCGC GCGCAACATG GAACCGGGCA
13381 TGTATGCCTC AAACCGGCCG TTTATCAACC GCCTAATGGA CTACTTGCAT CGCGCGGCCG
13441 CCGTGAACCC CGAGTATTTC ACCAATGCCA TCTTGAACCC GCACTGGCTA CCGCCCCCTG
13501 GTTTCTACAC CGGGGGATTC GAGGTGCCCG AGGGTAACGA TGGATTCCTC TGGGACGACA
13561 TAGACGACAG CGTGTTTTCC CCGCAACCGC AGACCCTGCT AGAGTTGCAA CAGCGCGAGC
13621 AGGCAGAGGC GGCGCTGCGA AAGGAAAGCT TCCGCAGGCC AAGCAGCTTG TCCGATCTAG
13681 GCGCTGCGGC CCCGCGGTCA GATGCTAGTA GCCCATTTCC AAGCTTGATA GGGTCTCTTA
13741 CCAGCACTCG CACCACCCGC CCGCGCCTGC TGGGCGAGGA GGAGTACCTA AACAACTCGC
13801 TGCTGCAGCC GCAGCGCGAA AAAAACCTGC CTCCGGCATT TCCCAACAAC GGGATAGAGA
13861 GCCTAGTGGA CAAGATGAGT AGATGGAAGA CGTACGCGCA GGAGCACAGG GACGTGCCAG
13921 GCCCGCGCCC GCCCACCCGT CGTCAAAGGC ACGACCGTCA GCGGGGTCTG GTGTGGGAGG
13981 ACGATGACTC GGCAGACGAC AGCAGCGTCC TGGATTTGGG AGGGAGTGGC AACCCGTTTG
14041 CGCACCTTCG CCCCAGGCTG GGGAGAATGT TTTAAAAAAA AAAAAGCATG ATGCAAAATA
14101 AAAAACTCAC CAAGGCCATG GCACCGAGCG TTGGTTTTCT TGTATTCCCC TTAGTATGCG
14161 GCGCGCGGCG ATGTATGAGG AAGGTCCTCC TCCCTCCTAC GAGAGTGTGG TGAGCGCGGC
14221 GCCAGTGGCG GCGGCGCTGG GTTCTCCCTT CGATGCTCCC CTGGACCCGC CGTTTGTGCC
14281 TCCGCGGTAC CTGCGGCCTA CCGGGGGGAG AAACAGCATC CGTTACTCTG AGTTGGCACC
14341 CCTATTCGAC ACCACCCGTG TGTACCTGGT GGACAACAAG TCAACGGATG TGGCATCCCT
14401 GAACTACCAG AACGACCACA GCAACTTTCT GACCACGGTC ATTCAAAACA ATGACTACAG
14461 CCCGGGGGAG GCAAGCACAC AGACCATCAA TCTTGACGAC CGGTCGCACT GGGGCGGCGA
14521 CCTGAAAACC ATCCTGCATA CCAACATGCC AAATGTGAAC GAGTTCATGT TTACCAATAA
14581 GTTTAAGGCG CGGGTGATGG TGTCGCGCTT GCCTACTAAG GACAATCAGG TGGAGCTGAA
14641 ATACGAGTGG GTGGAGTTCA CGCTGCCCGA GGGCAACTAC TCCGAGACCA TGACCATAGA
14701 CCTTATGAAC AACGCGATCG TGGAGCACTA CTTGAAAGTG GGCAGACAGA ACGGGGTTCT
14761 GGAAAGCGAC ATCGGGGTAA AGTTTGACAC CCGCAACTTC AGACTGGGGT TTGACCCCGT
14821 CACTGGTCTT GTCATGCCTG GGGTATATAC AAACGAAGCC TTCCATCCAG ACATCATTTT
14881 GCTGCCAGGA TGCGGGGTGG ACTTCACCCA CAGCCGCCTG AGCAACTTGT TGGGCATCCG
14941 CAAGCGGCAA CCCTTCCAGG AGGGCTTTAG GATCACCTAC GATGATCTGG AGGGTGGTAA
15001 CATTCCCGCA CTGTTGGATG TGGACGCCTA CCAGGCGAGC TTGAAAGATG ACACCGAACA
15061 GGGCGGGGGT GGCGCAGGCG GCAGCAACAG CAGTGGCAGC GGCGCGGAAG AGAACTCCAA
15121 CGCGGCAGCC GCGGCAATGC AGCCGGTGGA GGACATGAAC GATCATGCCA TTCGCGGCGA
15181 CACCTTTGCC ACACGGGCTG AGGAGAAGCG CGCTGAGGCC GAAGCAGCGG CCGAAGCTGC
15241 CGCCCCCGCT GCGCAACCCG AGGTCGAGAA GCCTCAGAAG AAACCGGTGA TCAAACCCCT
15301 GACAGAGGAC AGCAAGAAAC GCAGTTACAA CCTAATAAGC AATGACAGCA CCTTCACCCA
15361 GTACCGCAGC TGGTACCTTG CATACAACTA CGGCGACCCT CAGACCGGAA TCCGCTCATG
15421 GACCCTGCTT TGCACTCCTG ACGTAACCTG CGGCTCGGAG CAGGTCTACT GGTCGTTGCC
15481 AGACATGATG CAAGACCCCG TGACCTTCCG CTCCACGCGC CAGATCAGCA ACTTTCCGGT
15541 GGTGGGCGCC GAGCTGTTGC CCGTGCACTC CAAGAGCTTC TACAACGACC AGGCCGTCTA
15601 CTCCCAACTC ATCCGCCAGT TTACCTCTCT GACCCACGTG TTCAATCGCT TTCCCGAGAA
15661 CCAGATTTTG GCGCGCCCGC CAGCCCCCAC CATCACCACC GTCAGTGAAA ACGTTCCTGC
15721 TCTCACAGAT CACGGGACGC TACCGCTGCG CAACAGCATC GGAGGAGTCC AGCGAGTGAC
15781 CATTACTGAC GCCAGACGCC GCACCTGCCC CTACGTTTAC AAGGCCCTGG GCATAGTCTC
15841 GCCGCGCGTC CTATCGAGCC GCACTTTTTG AGCAAGCATG TCCATCCTTA TATCGCCCAG
15901 CAATAACACA GGCTGGGGCC TGCGCTTCCC AAGCAAGATG TTTGGCGGGG CCAAGAAGCG
15961 CTCCGACCAA CACCCAGTGC GCGTGCGCGG GCACTACCGC GCGCCCTGGG GCGCGCACAA
16021 ACGCGGCCGC ACTGGGCGCA CCACCGTCGA TGACGCCATC GACGCGGTGG TGGAGGAGGC
16081 GCGCAACTAC ACGCCCACGC CGCCACCAGT GTCCACAGTG GACGCGGCCA TTCAGACCGT
16141 GGTGCGCGGA GCCCGGCGCT ATGCTAAAAT GAAGAGACGG CGGAGGCGCG TAGCACGTCG
16201 CCACCGCCGC CGACCCGGCA CTGCCGCCCA ACGCGCGGCG GCGGCCCTGC TTAACCGCGC
16261 ACGTCGCACC GGCCGACGGG CGGCCATGCG GGCCGCTCGA AGGCTGGCCG CGGGTATTGT
16321 CACTGTGCCC CCCAGGTCCA GGCGACGAGC GGCCGCCGCA GCAGCCGCGG CCATTAGTGC
16381 TATGACTCAG GGTCGCAGGG GCAACGTGTA TTGGGTGCGC GACTCGGTTA GCGGCCTGCG
16441 CGTGCCCGTG CGCACCCGCC CCCCGCGCAA CTAGATTGCA AGAAAAAACT ACTTAGACTC

FIG. 8E

16501 GTACTGTTGT ATGTATCCAG CGGCGGCGGC GCGCAACGAA GCTATGTCCA AGCGCAAAAT
16561 CAAAGAAGAG ATGCTCCAGG TCATCGCGCC GGAGATCTAT GGCCCCCCGA AGAAGGAAGA
16621 GCAGGATTAC AAGCCCCGAA AGCTAAAGCG GGTCAAAAAG AAAAAGAAAG ATGATGATGA
16681 TGAACTTGAC GACGAGGTGG AACTGCTGCA CGCTACCGCG CCCAGGCGAC GGGTACAGTG
16741 GAAAGGTCGA CGCGTAAAAC GTGTTTTGCG ACCCGGCACC ACCGTAGTCT TTACGCCCGG
16801 TGAGCGCTCC ACCCGCACCT ACAAGCGCGT GTATGATGAG GTGTACGGCG ACGAGGACCT
16861 GCTTGAGCAG GCCAACGAGC GCCTCGGGGA GTTTGCCTAC GGAAAGCGGC ATAAGGACAT
16921 GCTGGCGTTG CCGCTGGACG AGGGCAACCC AACACCTAGC CTAAAGCCCG TAACACTGCA
16981 GCAGGTGCTG CCCGCGCTTG CACCGTCCGA AGAAAAGCGC GGCCTAAAGC GCGAGTCTGG
17041 TGACTTGGCA CCCACCGTGC AGCTGATGGT ACCCAAGCGC CAGCGACTGG AAGATGTCTT
17101 GGAAAAAATG ACCGTGGAAC CTGGGCTGGA GCCCGAGGTC CGCGTGCGGC CAATCAAGCA
17161 GGTGGCGCCG GGACTGGGCG TGCAGACCGT GGACGTTCAG ATACCCACTA CCAGTAGCAC
17221 CAGTATTGCC ACCGCCACAG AGGGCATGGA GACACAAACG TCCCCGGTTG CCTCAGCGGT
17281 GGCGGATGCC GCGGTGCAGG CGGTCGCTGC GGCCGCGTCC AAGACCTCTA CGGAGGTGCA
17341 AACGGACCCG TGGATGTTTC GCGTTTCAGC CCCCCGGCGC CCGCGCGGTT CGAGGAAGTA
17401 CGGCGCCGCC AGCGCGCTAC TGCCCGAATA TGCCCTACAT CCTTCCATTG CGCCTACCCC
17461 CGGCTATCGT GGCTACACCT ACCGCCCCAG AAGACGAGCA ACTACCCGAC GCCGAACCAC
17521 CACTGGAACC CGCCGCCGCC GTCGCCGTCG CCAGCCCGTG CTGGCCCCGA TTTCCGTGCG
17581 CAGGGTGGCT CGCGAAGGAG GCAGGACCCT GGTGCTGCCA ACAGCGCGCT ACCACCCCAG
17641 CATCGTTTAA AAGCCGGTCT TTGTGGTTCT TGCAGATATG GCCCTCACCT GCCGCCTCCG
17701 TTTCCCGGTG CCGGGATTCC GAGGAAGAAT GCACCGTAGG AGGGGCATGG CCGGCCACGG
17761 CCTGACGGGC GGCATGCGTC GTGCGCACCA CCGGCGGCGG CGCGCGTCGC ACCGTCGCAT
17821 GCGCGGCGGT ATCCTGCCCC TCCTTATTCC ACTGATCGCC GCGGCGATTG GCGCCGTGCC
17881 CGGAATTGCA TCCGTGGCCT TGCAGGCGCA GAGACACTGA TTAAAAACAA GTTGCATGTG
17941 GAAAAATCAA AATAAAAAGT CTGGACTCTC ACGCTCGCTT GGTCCTGTAA CTATTTTGTA
18001 GAATGGAAGA CATCAACTTT GCGTCTCTGG CCCCGCGACA CGGCTCGCGC CCGTTCATGG
18061 GAAACTGGCA AGATATCGGC ACCAGCAATA TGAGCGGTGG CGCCTTCAGC TGGGGCTCGC
18121 TGTGGAGCGG CATTAAAAAT TTCGGTTCCA CCGTTAAGAA CTATGGCAGC AAGGCCTGGA
18181 ACAGCAGCAC AGGCCAGATG CTGAGGGATA AGTTGAAAGA GCAAAATTTC CAACAAAAGG
18241 TGGTAGATGG CCTGGCCTCT GGCATTAGCG GGGTGGTGGA CCTGGCCAAC CAGGCAGTGC
18301 AAAATAAGAT TAACAGTAAG CTTGATCCCC GCCCTCCCGT AGAGGAGCCT CCACCGGCCG
18361 TGGAGACAGT GTCTCCAGAG GGGCGTGGCG AAAAGCGTCC GCGCCCCGAC AGGGAAGAAA
18421 CTCTGGTGAC GCAAATAGAC GAGCCTCCCT CGTACGAGGA GGCACTAAAG CAAGGCCTGC
18481 CCACCACCCG TCCCATCGCG CCCATGGCTA CCGGAGTGCT GGGCCAGCAC ACACCCGTAA
18541 CGCTGGACCT GCCTCCCCCC GCCGACACCC AGCAGAAACC TGTGCTGCCA GGCCCGACCG
18601 CCGTTGTTGT AACCCGTCCT AGCCGCGCGT CCCTGCGCCG CGCCGCCAGC GGTCCGCGAT
18661 CGTTGCGGCC CGTAGCCAGT GGCAACTGGC AAAGCACACT GAACAGCATC GTGGGTCTGG
18721 GGGTGCAATC CCTGAAGCGC CGACGATGCT TCTGAATAGC TAACGTGTCG TATGTGTGTC
18781 ATGTATGCGT CCATGTCGCC GCCAGAGGAG CTGCTGAGCC GCCGCGCGCC CGCTTTCCAA
18841 GATGGCTACC CCTTCGATGA TGCCGCAGTG GTCTTACATG CACATCTCGG GCCAGGACGC
18901 CTCGGAGTAC CTGAGCCCCG GGCTGGTGCA GTTTGCCCGC GCCACCGAGA CGTACTTCAG
18961 CCTGAATAAC AAGTTTAGAA ACCCCACGGT GGCGCCTACG CACGACGTGA CCACAGACCG
19021 GTCCCAGCGT TTGACGCTGC GGTTCATCCC TGTGGACCGT GAGGATACTG CGTACTCGTA
19081 CAAGGCGCGG TTCACCCTAG CTGTGGGTGA TAACCGTGTG CTGGACATGG CTTCCACGTA
19141 CTTTGACATC CGCGGCGTGC TGGACAGGGG CCCTACTTTT AAGCCCTACT CTGGCACTGC
19201 CTACAACGCC CTGGCTCCCA AGGGTGCCCC AAATCCTTGC GAATGGGATG AAGCTGCTAC
19261 TGCTCTTGAA ATAAACCTAG AAGAAGAGGA CGATGACAAC GAAGACGAAG TAGACGAGCA
19321 AGCTGAGCAG CAAAAAACTC ACGTATTTGG GCAGGCGCCT TATTCTGGTA TAAATATTAC
19381 AAAGGAGGGT ATTCAAATAG GTGTCGAAGG TCAAACACCT AAATATGCCG ATAAAACATT
19441 TCAACCTGAA CCTCAAATAG GAGAATCTCA GTGGTACGAA ACTGAAATTA ATCATGCAGC
19501 TGGGAGAGTC CTTAAAAAGA CTACCCCAAT GAAACCATGT TACGGTTCAT ATGCAAAACC
19561 CACAAATGAA AATGGAGGGC AAGGCATTCT TGTAAAGCAA CAAAATGGAA AGCTAGAAAG
19621 TCAAGTGGAA ATGCAATTTT TCTCAACTAC TGAGGCGACC GCAGGCAATG GTGATAACTT
19681 GACTCCTAAA GTGGTATTGT ACAGTGAAGA TGTAGATATA GAAACCCCAG ACACTCATAT
19741 TTCTTACATG CCCACTATTA AGGAAGGTAA CTCACGAGAA CTAATGGGCC AACAATCTAT

FIG. 8F

19801 GCCCAACAGG CCTAATTACA TTGCTTTTAG GGACAATTTT ATTGGTCTAA TGTATTACAA
19861 CAGCACGGGT AATATGGGTG TTCTGGCGGG CCAAGCATCG CAGTTGAATG CTGTTGTAGA
19921 TTTGCAAGAC AGAAACACAG AGCTTTCATA CCAGCTTTTG CTTGATTCCA TTGGTGATAG
19981 AACCAGGTAC TTTTCTATGT GGAATCAGGC TGTTGACAGC TATGATCCAG ATGTTAGAAT
20041 TATTGAAAAT CATGGAACTG AAGATGAACT TCCAAATTAC TGCTTTCCAC TGGGAGGTGT
20101 GATTAATACA GAGACTCTTA CCAAGGTAAA ACCTAAAACA GGTCAGGAAA ATGGATGGGA
20161 AAAAGATGCT ACAGAATTTT CAGATAAAAA TGAAATAAGA GTTGGAAATA ATTTTGCCAT
20221 GGAAATCAAT CTAAATGCCA ACCTGTGGAG AAATTTCCTG TACTCCAACA TAGCGCTGTA
20281 TTTGCCCGAC AAGCTAAAGT ACAGTCCTTC CAACGTAAAA ATTTCTGATA ACCCAAACAC
20341 CTACGACTAC ATGAACAAGC GAGTGGTGGC TCCCGGGTTA GTGGACTGCT ACATTAACCT
20401 TGGAGCACGC TGGTCCCTTG ACTATATGGA CAACGTCAAC CCATTTAACC ACCACCGCAA
20461 TGCTGGCCTG CGCTACCGCT CAATGTTGCT GGGCAATGGT CGCTATGTGC CCTTCCACAT
20521 CCAGGTGCCT CAGAAGTTCT TTGCCATTAA AAACCTCCTT CTCCTGCCGG GCTCATACAC
20581 CTACGAGTGG AACTTCAGGA AGGATGTTAA CATGGTTCTG CAGAGCTCCC TAGGAAATGA
20641 CCTAAGGGTT GACGGAGCCA GCATTAAGTT TGATAGCATT TGCCTTTACG CCACCTTCTT
20701 CCCCATGGCC CACAACACCG CCTCCACGCT TGAGGCCATG CTTAGAAACG ACACCAACGA
20761 CCAGTCCTTT AACGACTATC TCTCCGCCGC CAACATGCTC TACCCTATAC CCGCCAACGC
20821 TACCAACGTG CCCATATCCA TCCCCTCCCG CAACTGGGCG GCTTTCCGCG GCTGGGCCTT
20881 CACGCGCCTT AAGACTAAGG AAACCCCATC ACTGGGCTCG GGCTACGACC CTTATTACAC
20941 CTACTCTGGC TCTATACCCT ACCTAGATGG AACCTTTTAC CTCAACCACA CCTTTAAGAA
21001 GGTGGCCATT ACCTTTGACT CTTCTGTCAG CTGGCCTGGC AATGACCGCC TGCTTACCCC
21061 CAACGAGTTT GAAATTAAGC GCTCAGTTGA CGGGGAGGGT TACAACGTTG CCCAGTGTAA
21121 CATGACCAAA GACTGGTTCC TGGTACAAAT GCTAGCTAAC TACAACATTG GCTACCAGGG
21181 CTTCTATATC CCAGAGAGCT ACAAGGACCG CATGTACTCC TTCTTTAGAA ACTTCCAGCC
21241 CATGAGCCGT CAGGTGGTGG ATGATACTAA ATACAAGGAC TACCAACAGG TGGGCATCCT
21301 ACACCAACAC AACAACTCTG GATTTGTTGG CTACCTTGCC CCCACCATGC GCGAAGGACA
21361 GGCCTACCCT GCTAACTTCC CCTATCCGCT TATAGGCAAG ACCGCAGTTG ACAGCATTAC
21421 CCAGAAAAAG TTTCTTTGCG ATCGCACCCT TTGGCGCATC CCATTCTCCA GTAACTTTAT
21481 GTCCATGGGC GCACTCACAG ACCTGGGCCA AAACCTTCTC TACGCCAACT CCGCCCACGC
21541 GCTAGACATG ACTTTTGAGG TGGATCCCAT GGACGAGCCC ACCCTTCTTT ATGTTTTGTT
21601 TGAAGTCTTT GACGTGGTCC GTGTGCACCG GCCGCACCGC GGCGTCATCG AAACCGTGTA
21661 CCTGCGCACG CCCTTCTCGG CCGGCAACGC CACAACATAA AGAAGCAAGC AACATCAACA
21721 ACAGCTGCCG CCATGGGCTC CAGTGAGCAG GAACTGAAAG CCATTGTCAA AGATCTTGGT
21781 TGTGGGCCAT ATTTTTTGGG CACCTATGAC AAGCGCTTTC CAGGCTTTGT TTCTCCACAC
21841 AAGCTCGCCT GCGCCATAGT CAATACGGCC GGTCGCGAGA CTGGGGGCGT ACACTGGATG
21901 GCCTTTGCCT GGAACCCGCA CTCAAAAACA TGCTACCTCT TTGAGCCCTT TGGCTTTTCT
21961 GACCAGCGAC TCAAGCAGGT TTACCAGTTT GAGTACGAGT CACTCCTGCG CCGTAGCGCC
22021 ATTGCTTCTT CCCCCGACCG CTGTATAACG CTGGAAAAGT CCACCCAAAG CGTACAGGGG
22081 CCCAACTCGG CCGCCTGTGG ACTATTCTGC TGCATGTTTC TCCACGCCTT TGCCAACTGG
22141 CCCCAAACTC CCATGGATCA CAACCCCACC ATGAACCTTA TTACCGGGGT ACCCAACTCC
22201 ATGCTCAACA GTCCCCAGGT ACAGCCCACC CTGCGTCGCA ACCAGGAACA GCTCTACAGC
22261 TTCCTGGAGC GCCACTCGCC CTACTTCCGC AGCCACAGTG CGCAGATTAG GAGCGCCACT
22321 TCTTTTTGTC ACTTGAAAAA CATGTAAAAA TAATGTACTA GAGACACTTT CAATAAAGGC
22381 AAATGCTTTT ATTTGTACAC TCTCGGGTGA TTATTTACCC CCACCCTTGC CGTCTGCGCC
22441 GTTTAAAAAT CAAAGGGGTT CTGCCGCGCA TCGCTATGCG CCACTGGCAG GGACACGTTG
22501 CGATACTGGT GTTTAGTGCT CCACTTAAAC TCAGGCACAA CCATCCGCGG CAGCTCGGTG
22561 AAGTTTTCAC TCCACAGGCT GCGCACCATC ACCAACGCGT TTAGCAGGTC GGGCGCCGAT
22621 ATCTTGAAGT CGCAGTTGGG GCCTCCGCCC TGCGCGCGCG AGTTGCGATA CACAGGGTTG
22681 CAGCACTGGA ACACTATCAG CGCCGGGTGG TGCACGCTGG CCAGCACGCT CTTGTCGGAG
22741 ATCAGATCCG CGTCCAGGTC CTCCGCGTTG CTCAGGGCGA ACGGAGTCAA CTTTGGTAGC
22801 TGCCTTCCCA AAAAGGGCGC GTGCCCAGGC TTTGAGTTGC ACTCGCACCG TAGTGGCATC
22861 AAAAGGTGAC CGTGCCCGGT CTGGGCGTTA GGATACAGCG CCTGCATAAA AGCCTTGATC
22921 TGCTTAAAAG CCACCTGAGC CTTTGCGCCT TCAGAGAAGA ACATGCCGCA AGACTTGCCG
22981 GAAAACTGAT TGGCCGGACA GGCCGCGTCG TGCACGCAGC ACCTTGCGTC GGTGTTGGAG
23041 ATCTGCACCA CATTTCGGCC CCACCGGTTC TTCACGATCT TGGCCTTGCT AGACTGCTCC

FIG. 8G

```
23101 TTCAGCGCGC GCTGCCCGTT TTCGCTCGTC ACATCCATTT CAATCACGTG CTCCTTATTT
23161 ATCATAATGC TTCCGTGTAG ACACTTAAGC TCGCCTTCGA TCTCAGCGCA GCGGTGCAGC
23221 CACAACGCGC AGCCCGTGGG CTCGTGATGC TTGTAGGTCA CCTCTGCAAA CGACTGCAGG
23281 TACGCCTGCA GGAATCGCCC CATCATCGTC ACAAAGGTCT TGTTGCTGGT GAAGGTCAGC
23341 TGCAACCCGC GGTGCTCCTC GTTCAGCCAG GTCTTGCATA CGGCCGCCAG AGCTTCCACT
23401 TGGTCAGGCA GTAGTTTGAA GTTCGCCTTT AGATCGTTAT CCACGTGGTA CTTGTCCATC
23461 AGCGCGCGCG CAGCCTCCAT GCCCTTCTCC CACGCAGACA CGATCGGCAC ACTCAGCGGG
23521 TTCATCACCG TAATTTCACT TTCCGCTTCG CTGGGCTCTT CCTCTTCCTC TTGCGTCCGC
23581 ATACCACGCG CCACTGGGTC GTCTTCATTC AGCCGCCGCA CTGTGCGCTT ACCTCCTTTG
23641 CCATGCTTGA TTAGCACCGG TGGGTTGCTG AAACCCACCA TTTGTAGCGC CACATCTTCT
23701 CTTTCTTCCT CGCTGTCCAC GATTACCTCT GGTGATGGCG GGCGCTCGGG CTTGGGAGAA
23761 GGGCGCTTCT TTTTCTTCTT GGGCGCAATG GCCAAATCCG CCGCCGAGGT CGATGGCCGC
23821 GGGCTGGGTG TGCGCGGCAC CAGCGCGTCT TGTGATGAGT CTTCCTCGTC CTCGGACTCG
23881 ATACGCCGCC TCATCCGCTT TTTTGGGGGC GCCCGGGGAG GCGGCGGCGA CGGGGACGGG
23941 GACGACACGT CCTCCATGGT TGGGGGACGT CGCGCCGCAC CGCGTCCGCG CTCGGGGGTG
24001 GTTTCGCGCT GCTCCTCTTC CCGACTGGCC ATTTCCTTCT CCTATAGGCA GAAAAAGATC
24061 ATGGAGTCAG TCGAGAAGAA GGACAGCCTA ACCGCCCCCT CTGAGTTCGC CACCACCGCC
24121 TCCACCGATG CCGCCAACGC GCCTACCACC TTCCCCGTCG AGGCACCCCC GCTTGAGGAG
24181 GAGGAAGTGA TTATCGAGCA GGACCCAGGT TTTGTAAGCG AAGACGACGA GGACCGCTCA
24241 GTACCAACAG AGGATAAAAA GCAAGACCAG GACAACGCAG AGGCAAACGA GGAACAAGTC
24301 GGGCGGGGGG ACGAAAGGCA TGGCGACTAC CTAGATGTGG GAGACGACGT GCTGTTGAAG
24361 CATCTGCAGC GCCAGTGCGC CATTATCTGC GACGCGTTGC AAGAGCGCAG CGATGTGCCC
24421 CTCGCCATAG CGGATGTCAG CCTTGCCTAC GAACGCCACC TATTCTCACC GCGCGTACCC
24481 CCCAAACGCC AAGAAAACGG CACATGCGAG CCCAACCCGC GCCTCAACTT CTACCCCGTA
24541 TTTGCCGTGC CAGAGGTGCT TGCCACCTAT CACATCTTTT TCCAAAACTG CAAGATACCC
24601 CTATCCTGCC GTGCCAACCG CAGCCGAGCG GACAAGCAGC TGGCCTTGCG GCAGGGCGCT
24661 GTCATACCTG ATATCGCCTC GCTCAACGAA GTGCCAAAAA TCTTTGAGGG TCTTGGACGC
24721 GACGAGAAGC GCGCGGCAAA CGCTCTGCAA CAGGAAAACA GCGAAAATGA AAGTCACTCT
24781 GGAGTGTTGG TGGAACTCGA GGGTGACAAC GCGCGCCTAG CCGTACTAAA ACGCAGCATC
24841 GAGGTCACCC ACTTTGCCTA CCCGGCACTT AACCTACCCC CCAAGGTCAT GAGCACAGTC
24901 ATGAGTGAGC TGATCGTGCG CCGTGCGCAG CCCCTGGAGA GGGATGCAAA TTTGCAAGAA
24961 CAAACAGAGG AGGGCCTACC CGCAGTTGGC GACGAGCAGC TAGCGCGCTG GCTTCAAACG
25021 CGCGAGCCTG CCGACTTGGA GGAGCGACGC AAACTAATGA TGGCCGCAGT GCTCGTTACC
25081 GTGGAGCTTG AGTGCATGCA GCGGTTCTTT GCTGACCCGG AGATGCAGCG CAAGCTAGAG
25141 GAAACATTGC ACTACACCTT TCGACAGGGC TACGTACGCC AGGCCTGCAA GATCTCCAAC
25201 GTGGAGCTCT GCAACCTGGT CTCCTACCTT GGAATTTTGC ACGAAAACCG CCTTGGGCAA
25261 AACGTGCTTC ATTCCACGCT CAAGGGCGAG GCGCGCCGCG ACTACGTCCG CGACTGCGTT
25321 TACTTATTTC TATGCTACAC CTGGCAGACG GCCATGGGCG TTTGGCAGCA GTGCTTGGAG
25381 GAGTGCAACC TCAAGGAGCT GCAGAAACTG CTAAAGCAAA ACTTGAAGGA CCTATGGACG
25441 GCCTTCAACG AGCGCTCCGT GGCCGCGCAC CTGGCGGACA TCATTTTCCC CGAACGCCTG
25501 CTTAAAACCC TGCAACAGGG TCTGCCAGAC TTCACCAGTC AAAGCATGTT GCAGAACTTT
25561 AGGAACTTTA TCCTAGAGCG CTCAGGAATC TTGCCCGCCA CCTGCTGTGC ACTTCCTAGC
25621 GACTTTGTGC CCATTAAGTA CCGCGAATGC CCTCCGCCGC TTTGGGGCCA CTGCTACCTT
25681 CTGCAGCTAG CCAACTACCT TGCCTACCAC TCTGACATAA TGGAAGACGT GAGCGGTGAC
25741 GGTCTACTGG AGTGTCACTG TCGCTGCAAC CTATGCACCC CGCACCGCTC CCTGGTTTGC
25801 AATTCGCAGC TGCTTAACGA AAGTCAAATT ATCGGTACCT TTGAGCTGCA GGGTCCCTCG
25861 CCTGACGAAA AGTCCGCGGC TCCGGGGTTG AAACTCACTC CGGGGCTGTG GACGTCGGCT
25921 TACCTTCGCA AATTTGTACC TGAGGACTAC CACGCCCACG AGATTAGGTT CTACGAAGAC
25981 CAATCCCGCC CGCCAAATGC GGAGCTTACC GCCTGCGTCA TTACCCAGGG CCACATTCTT
26041 GGCCAATTGC AAGCCATCAA CAAAGCCCGC CAAGAGTTTC TGCTACGAAA GGGACGGGGG
26101 GTTTACTTGG ACCCCCAGTC CGGCGAGGAG CTCAACCCAA TCCCCCCGCC GCCGCAGCCC
26161 TATCAGCAGC AGCCGCGGGC CCTTGCTTCC CAGGATGGCA CCCAAAAAGA AGCTGCAGCT
26221 GCCGCCGCCA CCCACGGACG AGGAGGAATA CTGGGACAGT CAGGCAGAGG AGGTTTTGGA
26281 CGAGGAGGAG GAGGACATGA TGGAAGACTG GGAGAGCCTA GACGAGGAAG CTTCCGAGGT
26341 CGAAGAGGTG TCAGACGAAA CACCGTCACC CTCGGTCGCA TTCCCCTCGC CGGCGCCCCA
```

FIG. 8H

26401 GAAATCGGCA ACCGGTTCCA GCATGGCTAC AACCTCCGCT CCTCAGGCGC CGCCGGCACT
26461 GCCCGTTCGC CGACCCAACC GTAGATGGGA CACCACTGGA ACCAGGGCCG GTAAGTCCAA
26521 GCAGCCGCCG CCGTTAGCCC AAGAGCAACA ACAGCGCCAA GGCTACCGCT CATGGCGCGG
26581 GCACAAGAAC GCCATAGTTG CTTGCTTGCA AGACTGTGGG GGCAACATCT CCTTCGCCCG
26641 CCGCTTTCTT CTCTACCATC ACGGCGTGGC CTTCCCCCGT AACATCCTGC ATTACTACCG
26701 TCATCTCTAC AGCCCATACT GCACCGGCGG CAGCGGCAGC GGCAGCAACA GCAGCGGCCA
26761 CACAGAAGCA AAGGCGACCG GATAGCAAGA CTCTGACAAA GCCCAAGAAA TCCACAGCGG
26821 CGGCAGCAGC AGGAGGAGGA GCGCTGCGTC TGGCGCCCAA CGAACCCGTA TCGACCCGCG
26881 AGCTTAGAAA CAGGATTTTT CCCACTCTGT ATGCTATATT TCAACAGAGC AGGGGCCAAG
26941 AACAAGAGCT GAAAATAAAA AACAGGTCTC TGCGATCCCT CACCCGCAGC TGCCTGTATC
27001 ACAAAAGCGA AGATCAGCTT CGGCGCACGC TGGAAGACGC GGAGGCTCTC TTCAGTAAAT
27061 ACTGCGCGCT GACTCTTAAG GACTAGTTTC GCGCCCTTTC TCAAATTTAA GCGCGAAAAC
27121 TACGTCATCT CCAGCGGCCA CACCCGGCGC CAGCACCTGT CGTCAGCGCC ATTATGAGCA
27181 AGGAAATTCC CACGCCCTAC ATGTGGAGTT ACCAGCCACA AATGGGACTT GCGGCTGGAG
27241 CTGCCCAAGA CTACTCAACC CGAATAAACT ACATGAGCGC GGGACCCCAC ATGATATCCC
27301 GGGTCAACGG AATCCGCGCC CACCGAAACC GAATTCTCTT GGAACAGGCG GCTATTACCA
27361 CCACACCTCG TAATAACCTT AATCCCCGTA GTTGGCCCGC TGCCCTGGTG TACCAGGAAA
27421 GTCCCGCTCC CACCACTGTG GTACTTCCCA GAGACGCCCA GGCCGAAGTT CAGATGACTA
27481 ACTCAGGGGC GCAGCTTGCG GGCGGCTTTC GTCACAGGGT GCGGTCGCCC GGGCAGGGTA
27541 TAACTCACCT GACAATCAGA GGGCGAGGTA TTCAGCTCAA CGACGAGTCG GTGAGCTCCT
27601 CGCTTGGTCT CCGTCCGGAC GGGACATTTC AGATCGGCGG CGCCGGCCGT CCTTCATTCA
27661 CGCCTCGTCA GGCAATCCTA ACTCTGCAGA CCTCGTCCTC TGAGCCGCGC TCTGGAGGCA
27721 TTGGAACTCT GCAATTTATT GAGGAGTTTG TGCCATCGGT CTACTTTAAC CCCTTCTCGG
27781 GACCTCCCGG CCACTATCCG GATCAATTTA TTCCTAACTT TGACGCGGTA AAGGACTCGG
27841 CGGACGGCTA CGACTGAATG TTAAGTGGAG AGGCAGAGCA ACTGCGCCTG AAACACCTGG
27901 TCCACTGTCG CCGCCACAAG TGCTTTGCCC GCGACTCCGG TGAGTTTTGC TACTTTGAAT
27961 TGCCCGAGGA TCATATCGAG GGCCCGGCGC ACGGCGTCCG GCTTACCGCC CAGGGAGAGC
28021 TTGCCCGTAG CCTGATTCGG GAGTTTACCC AGCGCCCCCT GCTAGTTGAG CGGGACAGGG
28081 GACCCTGTGT TCTCACTGTG ATTTGCAACT GTCCTAACCT TGGATTACAT CAAGATCTTT
28141 GTTGCCATCT CTGTGCTGAG TATAATAAAT ACAGAAATTA AAATATACTG GGGCTCCTAT
28201 CGCCATCCTG TAAACGCCAC CGTCTTCACC CGCCCAAGCA AACCAAGGCG AACCTTACCT
28261 GGTACTTTTA ACATCTCTCC CTCTGTGATT TACAACAGTT TCAACCCAGA CGGAGTGAGT
28321 CTACGAGAGA ACCTCTCCGA GCTCAGCTAC TCCATCAGAA AAAACACCAC CCTCCTTACC
28381 TGCCGGGAAC GTACGAGTGC GTCACCGGCC GCTGCACCAC ACCTACCGCC TGACCGTAAA
28441 CCAGACTTTT TCCGGACAGA CCTCAATAAC TCTGTTTACC AGAACAGGAG GTGAGCTTAG
28501 AAAACCCTTA GGGTATTAGG CCAAAGGCGC AGCTACTGTG GGGTTTATGA ACAATTCAAG
28561 CAACTCTACG GGCTATTCTA ATTCAGGTTT CTCTAGAATC GGGGTTGGGG TTATTCTCTG
28621 TCTTGTGATT CTCTTTATTC TTATACTAAC GCTTCTCTGC CTAAGGCTCG CCGCCTGCTG
28681 TGTGCACATT TGCATTTATT GTCAGCTTTT TAAACGCTGG GGTCGCCACC CAAGATGATT
28741 AGGTACATAA TCCTAGGTTT ACTCACCCTT GCGTCAGCCC ACGGTACCAC CCAAAAGGTG
28801 GATTTTAAGG AGCCAGCCTG TAATGTTACA TTCGCAGCTG AAGCTAATGA GTGCACCACT
28861 CTTATAAAAT GCACCACAGA ACATGAAAAG CTGCTTATTC GCCACAAAAA CAAAATTGGC
28921 AAGTATGCTG TTTATGCTAT TTGGCAGCCA GGTGACACTA CAGAGTATAA TGTTACAGTT
28981 TTCCAGGGTA AAAGTCATAA AACTTTTATG TATACTTTTC CATTTTATGA AATGTGCGAC
29041 ATTACCATGT ACATGAGCAA ACAGTATAAG TTGTGGCCCC CACAAAATTG TGTGGAAAAC
29101 ACTGGCACTT TCTGCTGCAC TGCTATGCTA ATTACAGTGC TCGCTTTGGT CTGTACCCTA
29161 CTCTATATTA AATACAAAAG CAGACGCAGC TTTATTGAGG AAAAGAAAAT GCCTTAATTT
29221 ACTAAGTTAC AAAGCTAATG TCACCACTAA CTGCTTTACT CGCTGCTTGC AAAACAAATT
29281 CAAAAAGTTA GCATTATAAT TAGAATAGGA TTTAAACCCC CCGGTCATTT CCTGCTCAAT
29341 ACCATTCCCC TGAACAATTG ACTCTATGTG GGATATGCTC CAGCGCTACA ACCTTGAAGT
29401 CAGGCTTCCT GGATGTCAGC ATCTGACTTT GGCCAGCACC TGTCCCGCGG ATTTGTTCCA
29461 GTCCAACTAC AGCGACCCAC CCTAACAGAG ATGACCAACA CAACCAACGC GGCCGCCGCT
29521 ACCGGACTTA CATCTACCAC AAATACACCC CAAGTTTCTG CCTTTGTCAA TAACTGGGAT
29581 AACTTGGGCA TGTGGTGGTT CTCCATAGCG CTTATGTTTG TATGCCTTAT TATTATGTGG
29641 CTCATCTGCT GCCTAAAGCG CAAACGCGCC CGACCACCCA TCTATAGTCC CATCATTGTG

FIG. 8I

29701 CTACACCCAA ACAATGATGG AATCCATAGA TTGGACGGAC TGAAACACAT GTTCTTTTCT
29761 CTTACAGTAT GATTAAATGA GACATGATTC CTCGAGTTTT TATATTACTG ACCCTTGTTG
29821 CGCTTTTTTG TGCGTGCTCC ACATTGGCTG CGGTTTCTCA CATCGAAGTA GACTGCATTC
29881 CAGCCTTCAC AGTCTATTTG CTTTACGGAT TTGTCACCCT CACGCTCATC TGCAGCCTCA
29941 TCACTGTGGT CATCGCCTTT ATCCAGTGCA TTGACTGGGT CTGTGTGCGC TTTGCATATC
30001 TCAGACACCA TCCCCAGTAC AGGGACAGGA CTATAGCTGA GCTTCTTAGA ATTCTTTAAT
30061 TATGAAATTT ACTGTGACTT TTCTGCTGAT TATTTGCACC CTATCTGCGT TTTGTTCCCC
30121 GACCTCCAAG CCTCAAAGAC ATATATCATG CAGATTCACT CGTATATGGA ATATTCCAAG
30181 TTGCTACAAT GAAAAAAGCG ATCTTTCCGA AGCCTGGTTA TATGCAATCA TCTCTGTTAT
30241 GGTGTTCTGC AGTACCATCT TAGCCCTAGC TATATATCCC TACCTTGACA TTGGCTGGAA
30301 ACGAATAGAT GCCATGAACC ACCCAACTTT CCCCGCGCCC GCTATGCTTC CACTGCAACA
30361 AGTTGTTGCC GGCGGCTTTG TCCCAGCCAA TCAGCCTCGC CCCACTTCTC CCACCCCCAC
30421 TGAAATCAGC TACTTTAATC TAACAGGAGG AGATGACTGA CACCCTAGAT CTAGAAATGG
30481 ACGGAATTAT TACAGAGCAG CGCCTGCTAG AAAGACGCAG GGCAGCGGCC GAGCAACAGC
30541 GCATGAATCA AGAGCTCCAA GACATGGTTA ACTTGCACCA GTGCAAAAGG GGTATCTTTT
30601 GTCTGGTAAA GCAGGCCAAA GTCACCTACG ACAGTAATAC CACCGGACAC CGCCTTAGCT
30661 ACAAGTTGCC AACCAAGCGT CAGAAATTGG TGGTCATGGT GGGAGAAAAG CCCATTACCA
30721 TAACTCAGCA CTCGGTAGAA ACCGAAGGCT GCATTCACTC ACCTTGTCAA GGACCTGAGG
30781 ATCTCTGCAC CCTTATTAAG ACCCTGTGCG GTCTCAAAGA TCTTATTCCC TTTAACTAAT
30841 AAAAAAAAAT AATAAAGCAT CACTTACTTA AAATCAGTTA GCAAATTTCT GTCCAGTTTA
30901 TTCAGCAGCA CCTCCTTGCC CTCCTCCCAG CTCTGGTATT GCAGCTTCCT CCTGGCTGCA
30961 AACTTTCTCC ACAATCTAAA TGGAATGTCA GTTTCCTCCT GTTCCTGTCC ATCCGCACCC
31021 ACTATCTTCA TGTTGTTGCA GATGAAGCGC GCAAGACCGT CTGAAGATAC CTTCAACCCC
31081 GTGTATCCAT ATGACACGGA AACCGGTCCT CCAACTGTGC CTTTTCTTAC TCCTCCCTTT
31141 GTATCCCCCA ATGGGTTTCA AGAGAGTCCC CCTGGGGTAC TCTCTTTGCG CCTATCCGAA
31201 CCTCTAGTTA CCTCCAATGG CATGCTTGCG CTCAAAATGG GCAACGGCCT CTCTCTGGAC
31261 GAGGCCGGCA ACCTTACCTC CCAAAATGTA ACCACTGTGA GCCCACCTCT CAAAAAAACC
31321 AAGTCAAACA TAAACCTGGA AATATCTGCA CCCCTCACAG TTACCTCAGA AGCCCTAACT
31381 GTGGCTGCCG CCGCACCTCT AATGGTCGCG GGCAACACAC TCACCATGCA ATCACAGGCC
31441 CCGCTAACCG TGCACGACTC CAAACTTAGC ATTGCCACCC AAGGACCCCT CACAGTGTCA
31501 GAAGGAAAGC TAGCCCTGCA AACATCAGGC CCCCTCACCA CCACCGATAG CAGTACCCTT
31561 ACTATCACTG CCTCACCCCC TCTAACTACT GCCACTGGTA GCTTGGGCAT TGACTTGAAA
31621 GAGCCCATTT ATACACAAAA TGGAAAACTA GGACTAAAGT ACGGGGCTCC TTTGCATGTA
31681 ACAGACGACC TAAACACTTT GACCGTAGCA ACTGGTCCAG GTGTGACTAT TAATAATACT
31741 TCCTTGCAAA CTAAAGTTAC TGGAGCCTTG GGTTTTGATT CACAAGGCAA TATGCAACTT
31801 AATGTAGCAG GAGGACTAAG GATTGATTCT CAAAACAGAC GCCTTATACT TGATGTTAGT
31861 TATCCGTTTG ATGCTCAAAA CCAACTAAAT CTAAGACTAG GACAGGGCCC TCTTTTTATA
31921 AACTCAGCCC ACAACTTGGA TATTAACTAC AACAAAGGCC TTTACTTGTT TACAGCTTCA
31981 AACAATTCCA AAAAGCTTGA GGTTAACCTA AGCACTGCCA AGGGGTTGAT GTTTGACGCT
32041 ACAGCCATAG CCATTAATGC AGGAGATGGG CTTGAATTTG GTTCACCTAA TGCACCAAAC
32101 ACAAATCCCC TCAAAACAAA AATTGGCCAT GGCCTAGAAT TTGATTCAAA CAAGGCTATG
32161 GTTCCTAAAC TAGGAACTGG CCTTAGTTTT GACAGCACAG GTGCCATTAC AGTAGGAAAC
32221 AAAAATAATG ATAAGCTAAC TTTGTGGACC ACACCAGCTC CATCTCCTAA CTGTAGACTA
32281 AATGCAGAGA AAGATGCTAA ACTCACTTTG GTCTTAACAA AATGTGGCAG TCAAATACTT
32341 GCTACAGTTT CAGTTTTGGC TGTTAAAGGC AGTTTGGCTC CAATATCTGG AACAGTTCAA
32401 AGTGCTCATC TTATTATAAG ATTTGACGAA AATGGAGTGC TACTAAACAA TTCCTTCCTG
32461 GACCCAGAAT ATTGGAACTT TAGAAATGGA GATCTTACTG AAGGCACAGC CTATACAAAC
32521 GCTGTTGGAT TTATGCCTAA CCTATCAGCT TATCCAAAAT CTCACGGTAA AACTGCCAAA
32581 AGTAACATTG TCAGTCAAGT TTACTTAAAC GGAGACAAAA CTAAACCTGT AACACTAACC
32641 ATTACACTAA ACGGTACACA GGAAACAGGA GACACAACTC CAAGTGCATA CTCTATGTCA
32701 TTTTCATGGG ACTGGTCTGG CCACAACTAC ATTAATGAAA TATTTGCCAC ATCCTCTTAC
32761 ACTTTTTCAT ACATTGCCCA AGAATAAAGA ATCGTTTGTG TTATGTTTCA ACGTGTTTAT
32821 TTTTCAATTG CAGAAAATTT CAAGTCATTT TTCATTCAGT AGTATAGCCC CACCACCACA
32881 TAGCTTATAC AGATCACCGT ACCTTAATCA AACTCACAGA ACCCTAGTAT TCAACCTGCC
32941 ACCTCCCTCC CAACACACAG AGTACACAGT CCTTTCTCCC CGGCTGGCCT TAAAAAGCAT

FIG. 8J

33001 CATATCATGG GTAACAGACA TATTCTTAGG TGTTATATTC CACACGGTTT CCTGTCGAGC
33061 CAAACGCTCA TCAGTGATAT TAATAAACTC CCCGGGCAGC TCACTTAAGT TCATGTCGCT
33121 GTCCAGCTGC TGAGCCACAG GCTGCTGTCC AACTTGCGGT TGCTTAACGG GCGGCGAAGG
33181 AGAAGTCCAC GCCTACATGG GGGTAGAGTC ATAATCGTGC ATCAGGATAG GGCGGTGGTG
33241 CTGCAGCAGC GCGCGAATAA ACTGCTGCCG CCGCCGCTCC GTCCTGCAGG AATACAACAT
33301 GGCAGTGGTC TCCTCAGCGA TGATTCGCAC CGCCCGCAGC ATAAGGCGCC TTGTCCTCCG
33361 GGCACAGCAG CGCACCCTGA TCTCACTTAA ATCAGCACAG TAACTGCAGC ACAGCACCAC
33421 AATATTGTTC AAAATCCCAC AGTGCAAGGC GCTGTATCCA AAGCTCATGG CGGGGACCAC
33481 AGAACCCACG TGGCCATCAT ACCACAAGCG CAGGTAGATT AAGTGGCGAC CCCTCATAAA
33541 CACGCTGGAC ATAAACATTA CCTCTTTTGG CATGTTGTAA TTCACCACCT CCCGGTACCA
33601 TATAAACCTC TGATTAAACA TGGCGCCATC CACCACCATC CTAAACCAGC TGGCCAAAAC
33661 CTGCCCGCCG GCTATACACT GCAGGGAACC GGGACTGGAA CAATGACAGT GGAGAGCCCA
33721 GGACTCGTAA CCATGGATCA TCATGCTCGT CATGATATCA ATGTTGGCAC AACACAGGCA
33781 CACGTGCATA CACTTCCTCA GGATTACAAG CTCCTCCCGC GTTAGAACCA TATCCCAGGG
33841 AACAACCCAT TCCTGAATCA GCGTAAATCC CACACTGCAG GGAAGACCTC GCACGTAACT
33901 CACGTTGTGC ATTGTCAAAG TGTTACATTC GGGCAGCAGC GGATGATCCT CCAGTATGGT
33961 AGCGCGGGTT TCTGTCTCAA AAGGAGGTAG ACGATCCCTA CTGTACGGAG TGCGCCGAGA
34021 CAACCGAGAT CGTGTTGGTC GTAGTGTCAT GCCAAATGGA ACGCCGGACG TAGTCATATT
34081 TCCTGAAGCA AAACCAGGTG CGGGCGTGAC AAACAGATCT GCGTCTCCGG TCTCGCCGCT
34141 TAGATCGCTC TGTGTAGTAG TTGTAGTATA TCCACTCTCT CAAAGCATCC AGGCGCCCCC
34201 TGGCTTCGGG TTCTATGTAA ACTCCTTCAT GCGCCGCTGC CCTGATAACA TCCACCACCG
34261 CAGAATAAGC CACACCCAGC CAACCTACAC ATTCGTTCTG CGAGTCACAC ACGGGAGGAG
34321 CGGGAAGAGC TGGAAGAACC ATGTTTTTTT TTTTATTCCA AAAGATTATC CAAAACCTCA
34381 AAATGAAGAT CTATTAAGTG AACGCGCTCC CCTCCGGTGG CGTGGTCAAA CTCTACAGCC
34441 AAAGAACAGA TAATGGCATT TGTAAGATGT TGCACAATGG CTTCCAAAAG GCAAACGGCC
34501 CTCACGTCCA AGTGGACGTA AAGGCTAAAC CCTTCAGGGT GAATCTCCTC TATAAACATT
34561 CCAGCACCTT CAACCATGCC CAAATAATTC TCATCTCGCC ACCTTCTCAA TATATCTCTA
34621 AGCAAATCCC GAATATTAAG TCCGGCCATT GTAAAAATCT GCTCCAGAGC GCCCTCCACC
34681 TTCAGCCTCA AGCAGCGAAT CATGATTGCA AAAATTCAGG TTCCTCACAG ACCTGTATAA
34741 GATTCAAAAG CGGAACATTA ACAAAAATAC CGCGATCCCG TAGGTCCCTT CGCAGGGCCA
34801 GCTGAACATA ATCGTGCAGG TCTGCACGGA CCAGCGCGGC CACTTCCCCG CCAGGAACCT
34861 TGACAAAAGA ACCCACACTG ATTATGACAC GCATACTCGG AGCTATGCTA ACCAGCGTAG
34921 CCCCGATGTA AGCTTTGTTG CATGGGCGGC GATATAAAAT GCAAGGTGCT GCTCAAAAAA
34981 TCAGGCAAAG CCTCGCGCAA AAAAGAAAGC ACATCGTAGT CATGCTCATG CAGATAAAGG
35041 CAGGTAAGCT CCGGAACCAC CACAGAAAAA GACACCATTT TTCTCTCAAA CATGTCTGCG
35101 GGTTTCTGCA TAAACACAAA ATAAAATAAC AAAAAAACAT TTAAACATTA GAAGCCTGTC
35161 TTACAACAGG AAAAACAACC CTTATAAGCA TAAGACGGAC TACGGCCATG CCGGCGTGAC
35221 CGTAAAAAAA CTGGTCACCG TGATTAAAAA GCACCACCGA CAGCTCCTCG GTCATGTCCG
35281 GAGTCATAAT GTAAGACTCG GTAAACACAT CAGGTTGATT CATCGGTCAG TGCTAAAAAG
35341 CGACCGAAAT AGCCCGGGGG AATACATACC CGCAGGCGTA GAGACAACAT TACAGCCCCC
35401 ATAGGAGGTA TAACAAAATT AATAGGAGAG AAAAACACAT AAACACCTGA AAAACCCTCC
35461 TGCCTAGGCA AAATAGCACC CTCCCGCTCC AGAACAACAT ACAGCGCTTC ACAGCGGCAG
35521 CCTAACAGTC AGCCTTACCA GTAAAAAAGA AAACCTATTA AAAAAACACC ACTCGACACG
35581 GCACCAGCTC AATCAGTCAC AGTGTAAAAA AGGGCCAAGT GCAGAGCGAG TATATATAGG
35641 ACTAAAAAAT GACGTAACGG TTAAAGTCCA CAAAAAACAC CCAGAAAACC GCACGCGAAC
35701 CTACGCCCAG AAACGAAAGC CAAAAAACCC ACAACTTCCT CAAATCGTCA CTTCCGTTTT
35761 CCCACGTTAC GTAACTTCCC ATTTTAAGAA AACTACAATT CCCAACACAT ACAAGTTACT
35821 CCGCCCTAAA ACCTACGTCA CCCGCCCCGT TCCCACGCCC CGCGCCACGT CACAAACTCC
35881 ACCCCCTCAT TATCATATTG GCTTCAATCC AAAATAAGGT ATATTATTGA TGATG

FIG. 8K

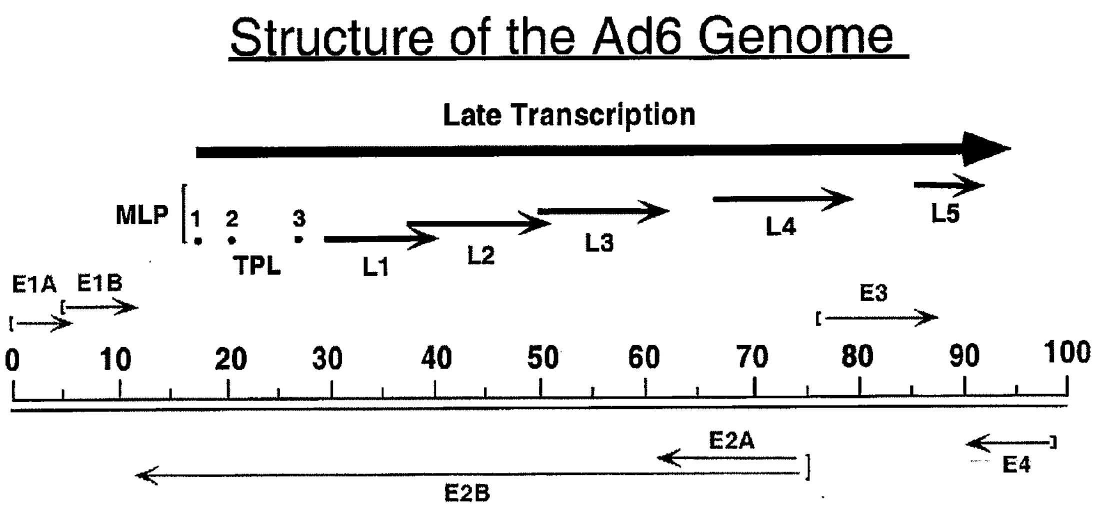

Structure of the Ad6 Genome
Late Transcription
MLP
1
2
3
TPL
L1
L2
L3
L4
L5
E1A
E1B
E3
0
10
20
30
40
50
60
70
80
90
100
E2A
E2B
E4

FIG. 9

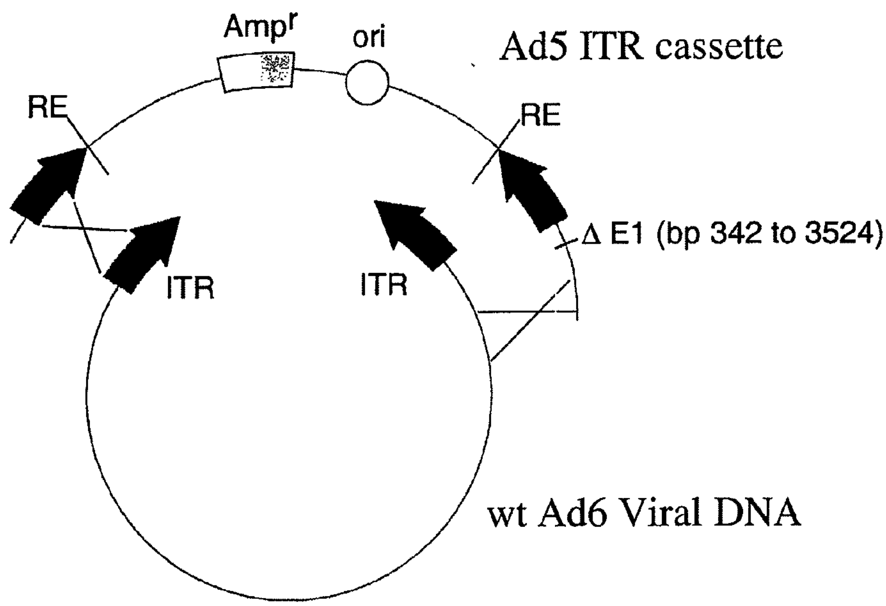

Ampr
ori
Ad5 ITR cassette
RE
RE
Δ E1 (bp 342 to 3524)
ITR
ITR
wt Ad6 Viral DNA

FIG. 10

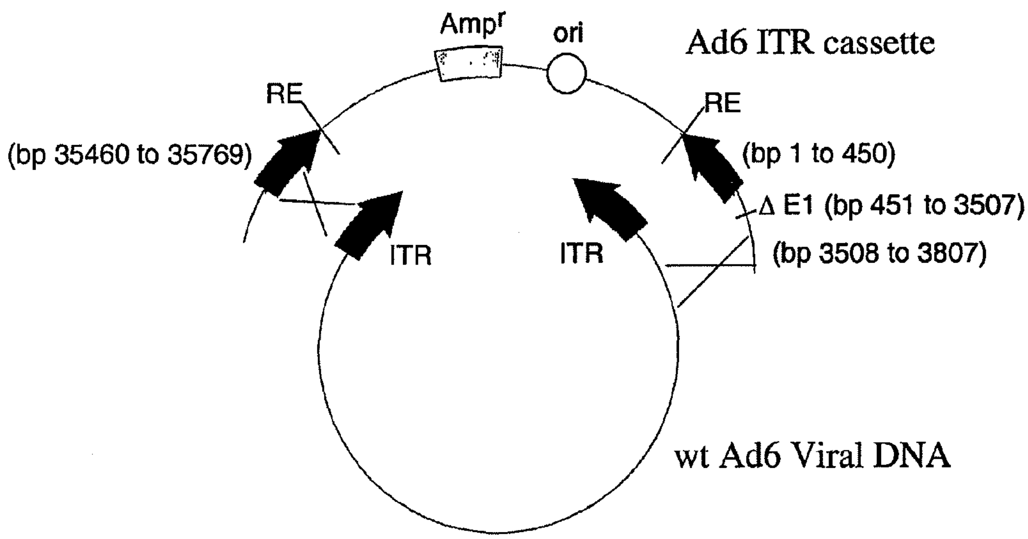
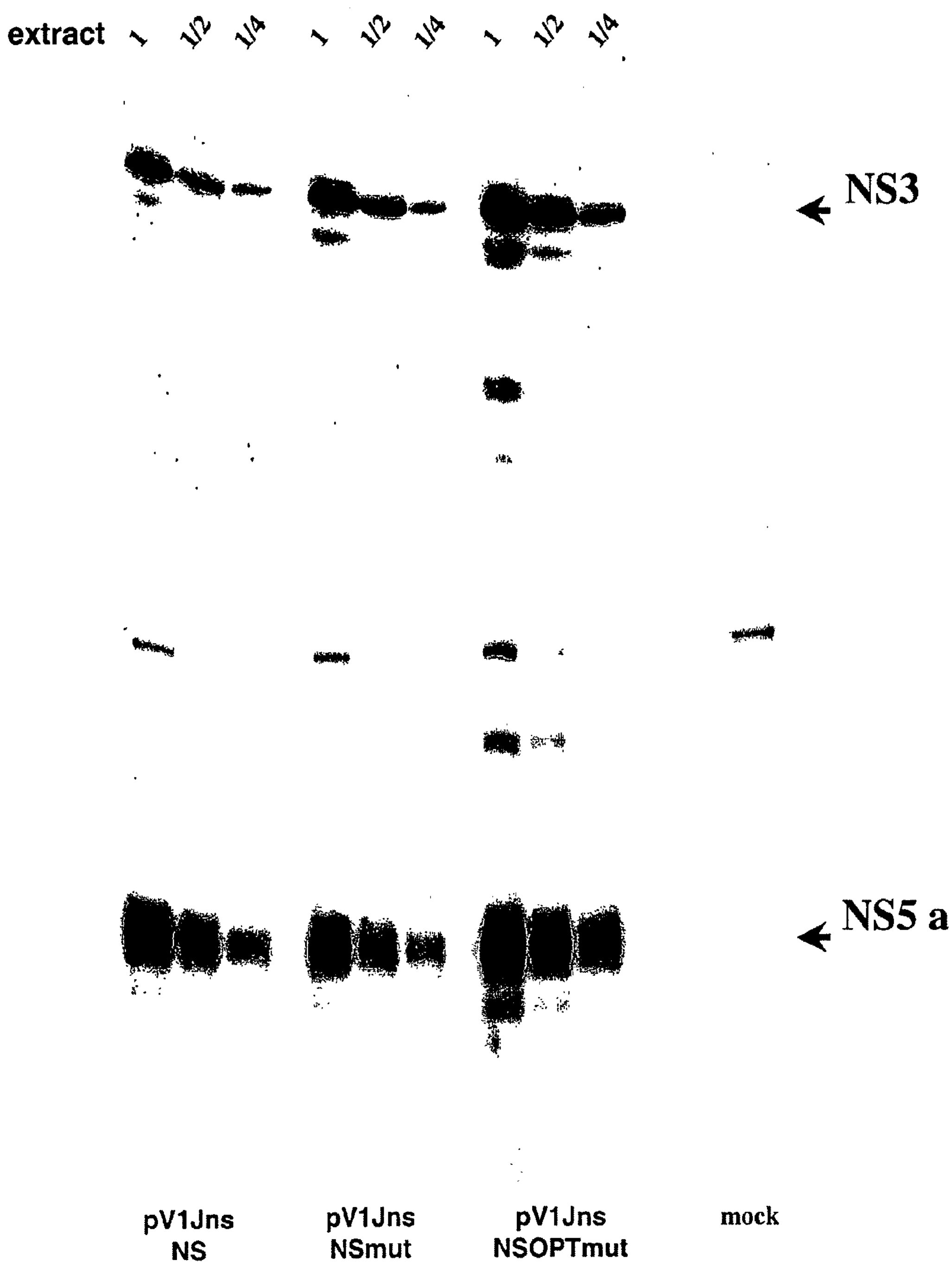

Amp^r
ori
Ad6 ITR cassette
RE
RE
(bp 35460 to 35769)
(bp 1 to 450)
Δ E1 (bp 451 to 3507)
(bp 3508 to 3807)
ITR
ITR
wt Ad6 Viral DNA

FIG. 11



Western blot on whole-cell extracts from 293 cells transfected with plasmid DNA expressing the different HCV NS cassettes. Mature NS3 and NS5A products were detected with specific antibodies.

FIG. 12

	mouse	Pep pool F(NS3p)	G(NS3h)	H(NS4)	I(NS5a)	L(NS35b)	M(NS5b)	1480(CD8 ep)	DMSO
pV1jns-NS	#31	41	135	19	44	25	17	137	8
	#32	121	783	77	144	13	22	604	4
	#33	8	32	3	11	6	6	43	3
	#34	16	139	13	47	31	25	151	2
	#35	21	101	40	32	21	20	75	1
	#36	18	26	24	25	5	7	29	6
	#37	19	73	15	39	8	20	49	2
	#38	133	575	74	345	75	63	515	5
	#39	40	183	10	85	14	9	148	2
	#40	66	465	29	111	15	16	189	0
	Geomean	33	146	21	57	15	16	123	na

	mouse	Pep pool F(NS3p)	G(NS3h)	H(NS4)	I(NS5a)	L(NS35b)	M(NS5b)	1480(CD8 ep)	DMSO
pV1jns-NSmut	#41	39	293	58	187	5	4	248	1
	#42	21	220	46	107	26	10	189	4
	#43	76	134	12	78	8	6	144	2
	#44	30	45	20	52	4	8	40	4
	#45	36	100	17	56	4	6	116	3
	#46	67	172	16	138	8	9	145	3
	#47	34	131	28	38	9	5	118	1
	#48	55	316	43	107	9	7	277	5
	#49	6	131	5	25	4	1	91	0
	#50	13	93	11	11	5	1	76	1
	Geomean	30	142	20	61	7	5	126	na

	mouse	Pep pool F(NS3p)	G(NS3h)	H(NS4)	I(NS5a)	L(NS35b)	M(NS5b)	1480(CD8 ep)	DMSO
V1jns-NSOPTmut	#51	53	409	34	84	11	25	271	4
	#52	140	660	65	276	23	36	377	2
	#53	58	553	48	105	23	18	564	1
	#54	50	105	35	134	10	16	80	2
	#55	14	80	11	35	4	7	91	6
	#56	14	342	30	101	23	14	207	1
	#57	63	325	66	239	17	24	123	1
	#58	75	542	66	168	127	93	191	0
	#59	65	468	40	124	18	23	344	4
	#60	27	142	48	16	7	8	77	0
	Geomean	45	295	40	99	16	20	188	na

IFNγ ELIspot on splenocytes from C57black6 mice immunized with two injections of 25μg DNA/dose with GET of plasmid vectors expressing the different HCV NS cassettes. Data are expressed as SFC/10^6 PBMC.

FIG. 13A

pV1jns-NS

mouse	F(NS3p)	G(NS3h)	H(NS4)	I(NS5a)	L(NS35b)	M(NS5b)	DMSO
	Pep pool						
#51	219	699	634	486	487	264	34
#52	67	302	347	167	111	87	9
#53	59	460	400	246	244	136	26
#54	139	817	685	236	547	223	24
#55	96	904	542	277	256	337	17
#56	225	603	686	156	350	240	56
#57	44	288	211	148	100	141	4
#58	37	262	221	53	58	62	3
#59	131	975	928	159	305	284	14
#60	93	475	464	77	206	113	12
geo mean	111	579	512	201	266	189	20

pV1jns-NSmut

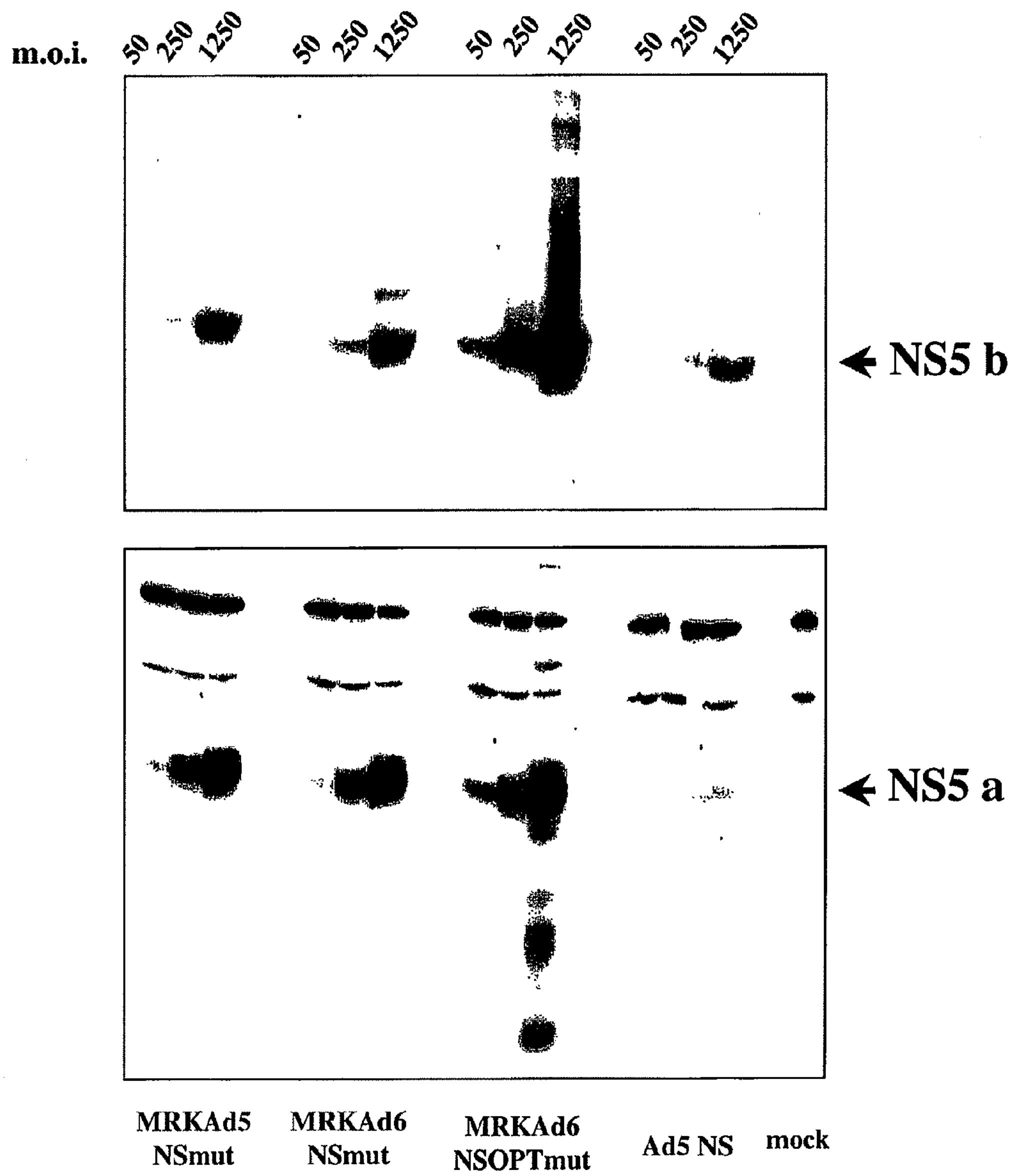
mouse	F(NS3p)	G(NS3h)	H(NS4)	I(NS5a)	L(NS35b)	M(NS5b)	DMSO
	Pep pool						
#61	72	840	515	219	278	249	19
#62	294	1881	1266	365	434	411	63
#63	73	415	422	103	141	99	41
#64	66	824	486	175	162	144	18
#66	24	313	168	53	47	42	5
#67	15	230	253	94	25	39	2
#68	53	354	252	89	101	86	15
#69	271	895	909	518	322	285	74
#70	417	1303	1186	468	557	267	34
geo mean	143	784	606	232	230	180	30

V1jns-NSOPTmut

mouse	F(NS3p)	G(NS3h)	H(NS4)	I(NS5a)	L(NS35b)	M(NS5b)	DMSO
	Pep pool						
#71	206	944	890	342	207	397	47
#72	393	1655	1151	575	626	401	72
#73	123	522	515	319	223	198	21
#74	500	1414	1419	878	1035	1122	137
#75	286	812	873	382	543	267	31
#76	224	1143	942	218	420	281	22
#77	95	643	630	169	385	218	15
#78	401	1302	1068	538	608	623	12
#79	108	1190	914	199	265	215	4
#80	122	511	546	189	286	190	13
geo mean	209	941	854	331	406	329	24

IFNγ ELIspot on splenocytes from BalbC mice immunized with two injections of 50μg DNA/dose with GET of plasmid vectors expressing the different HCV NS cassettes. Data are expressed as SFC/10^6 PBMC.

FIG. 13B



Western blot on whole-cell extracts from HeLa cells infected at different multiplicity of infection (m.o.i.; indicated at the top) with Adenovectors expressing the different HCV NS cassettes. Mature NS5B and NS5A products were detected with specific antibodies.

FIG. 14

Ad5-NS

mouse	F(NS3p)	G(NS3h)	H(NS4)	I(NS5a)	L+M(NS35b)	1480(CD8 ep)	DMSO
	Pep pool						
#1	14	492	9	27	10	554	7
#2	8	440	2	26	5	438	0
#3	12	92	5	12	7	73	4
#4	16	388	6	40	6	228	2
#6	8	210	4	31	3	238	3
#7	7	133	13	16	0	128	9
#8	11	342	25	55	22	267	12
#9	5	345	0	45	5	285	3
#10	22	888	3	65	25	799	1
Geomean	10	305	na	31	na	269	na

MRKAd5-NSmut

mouse	F(NS3p)	G(NS3h)	H(NS4)	I(NS5a)	L+M(NS35b)	1480(CD8 ep)	DMSO
	Pep pool						
#11	14	1009	13	75	7	751	6
#12	15	695	3	39	9	552	1
#13	12	389	4	20	7	352	3
#14	7	459	6	50	1	274	1
#15	5	549	3	22	6	485	0
#16	10	631	1	6	4	600	3
#17	5	257	3	9	1	245	3
#18	13	659	6	43	7	555	1
#19	12	758	1	37	5	669	0
#20	22	1380	5	163	8	1003	4
Geomean	10	615	3	31	4	504	na

MRKAd6-NSmut

mouse	F(NS3p)	G(NS3h)	H(NS4)	I(NS5a)	L+M(NS35b)	1480(CD8 ep)	DMSO
	Pep pool						
#21	6	584	5	27	4	491	2
#22	6	231	3	12	3	235	0
#23	8	482	1	18	1	511	0
#24	14	1120	6	38	10	1004	5
#25	1	311	3	9	0	382	1
#26	29	903	3	60	5	751	5
#27	35	1573	4	40	4	1277	4
#28	7	406	5	15	1	443	3
#29	4	461	3	12	3	515	3
Geomean	8	567	3	21	na	554	na

IFNγ ELISPOT on splenocytes from C57black6 mice immunized with two injections of 10^9 vp/dose of Adenovectors expressing the different HCV NS cassettes. Data are expressed as SFC/10^6 PBMC.

FIG. 15

	Ad5-NS 10^{10} vp/dose		
Pep pools	*96074*	*134T*	*063Q*
F (NS3p)	374	11	74
G (NS3h)	359	1070	1455
H (NS4)	376	30	64
I (NS5a)	240	40	63
L (NS5b)	226	29	121
M (NS5b)	511	23	35
DMSO	*128*	3	31

	MRK Ad6-NSmut 10^{10} vp/dose		
Pep pools	*S207*	*035Q*	*057Q*
F (NS3p)	363	382	150
G (NS3h)	180	316	119
H (NS4)	126	113	62
I (NS5a)	1780	688	114
L (NS5b)	447	111	81
M (NS5b)	153	38	16
DMSO	9	6	9

IFNγ ELISPOT on PBMC from Rhesus monkeys immunized with one injection of 10^{10} vp/dose of Adenovectors expressing the different HCV NS cassettes. Data are expressed as SFC/10^6 PBMC.

FIG. 16A

Pep pools	MRK Ad5-NSmut 10^{10} vp/dose		
	S201	*075Q*	*137Q*
F (NS3p)	928	69	254
G (NS3h)	317	436	98
H (NS4)	56	101	45
I (NS5a)	1530	1100	413
L (NS5b)	149	23	92
M (NS5b)	398	32	80
DMSO	29	6	29

Pep pools	MRK Ad6-NSOPTmut 10^{10} vp/dose		
	98D209	*106Q*	*113Q*
F (NS3p)	3110	263	404
G (NS3h)	2115	642	1008
H (NS4)	373	72	19
I (NS5a)	103	37	347
L (NS5b)	149	22	10
M (NS5b)	314	428	19
DMSO	0	1	3

IFNγ ELISPOT on PBMC from Rhesus monkeys immunized with one injection of 10^{10} vp/dose of Adenovectors expressing the different HCV NS cassettes. Data are expressed as SFC/10^6 PBMC.

FIG. 16B

Pep pools	Ad5-NS 10^{11} vp/dose			
	99C008	*97N104*	*97X008*	*99C026*
F (NS3p)	28	1026	579	889
G (NS3h)	1279	188	103	2453
H (NS4)	18	39	138	109
I (NS5a)	131	1068	172	141
L (NS5b)	78	144	103	32
M (NS5b)	24	68	47	84
DMSO	3	16	1	19

Pep pools	MRKAd6-NSmut 10^{11} vp/dose			
	98C047	*97C055*	*93G*	*97X014*
F (NS3p)	477	25	93	1022
G (NS3h)	959	398	81	1513
H (NS4)	36	14	99	53
I (NS5a)	171	45	1237	98
L (NS5b)	18	32	23	51
M (NS5b)	88	4	13	40
DMSO	8	3	1	5

IFNγ ELISPOT on PBMC from Rhesus monkeys immunized with two injections of 10^{11} vp/dose of Adenovectors expressing the different HCV NS cassettes. Data are expressed as SFC/10^6 PBMC.

FIG. 16C

	MRKAd5-NSmut 10^{11} vp/dose			
Pep pools	*99C059*	*99C060*	*97X009*	*96069*
F (NS3p)	28	81	1308	1618
G (NS3h)	2600	161	1008	123
H (NS4)	31	74	101	40
I (NS5a)	181	99	69	96
L (NS5b)	24	31	40	20
M (NS5b)	11	58	38	164
DMSO	6	15	1	16

IFNγ ELISPOT on PBMC from Rhesus monkeys immunized with two injections of 10^{11} vp/dose of Adenovectors expressing the different HCV NS cassettes. Data are expressed as SFC/10^6 PBMC.

FIG. 16D

Pep pools	MRK Ad5-NSmut 10^{10} vp/dose		
	S201	*075Q*	*137Q*
pool F (NS3p)	881	1755	73
pool G (NS3h)	573		
pool H (NS4)		3541	
pool I (NS5a)	2094		39
pool L (NS5b)			
pool M (NS5b)	756		
DMSO	*319*	*117*	*44*

Pep pools	MRK Ad6-NSOPTmut 10^{10} vp/dose		
	98D209	*106Q*	*113Q*
pool F (NS3p)	5073	84	952
pool G (NS3h)	2376	160	3325
pool H (NS4)	700		
pool I (NS5a)			1106
pool L (NS5b)			
pool M (NS5b)	530	706	
DMSO	43	47	28

Pep pools	MRK Ad6-NSmut 10^{10} vp/dose		
	S207	*035Q*	*057Q*
pool F (NS3p)	118	480	
pool G (NS3h)		196	
pool H (NS4)			
pool I (NS5a)	3340	933	
pool L (NS5b)	118		
pool M (NS5b)			
DMSO	145	34	

IFNγ ICS on PBMC from Rhesus monkeys immunized with two injections at four weeks interval with 10^{10} vp/dose of Adenovectors expressing the different HCV NS cassettes. Data are expressed as number of positive IFNγ/CD3/CD8 per 10^6 lymphocytes.

FIG. 17A

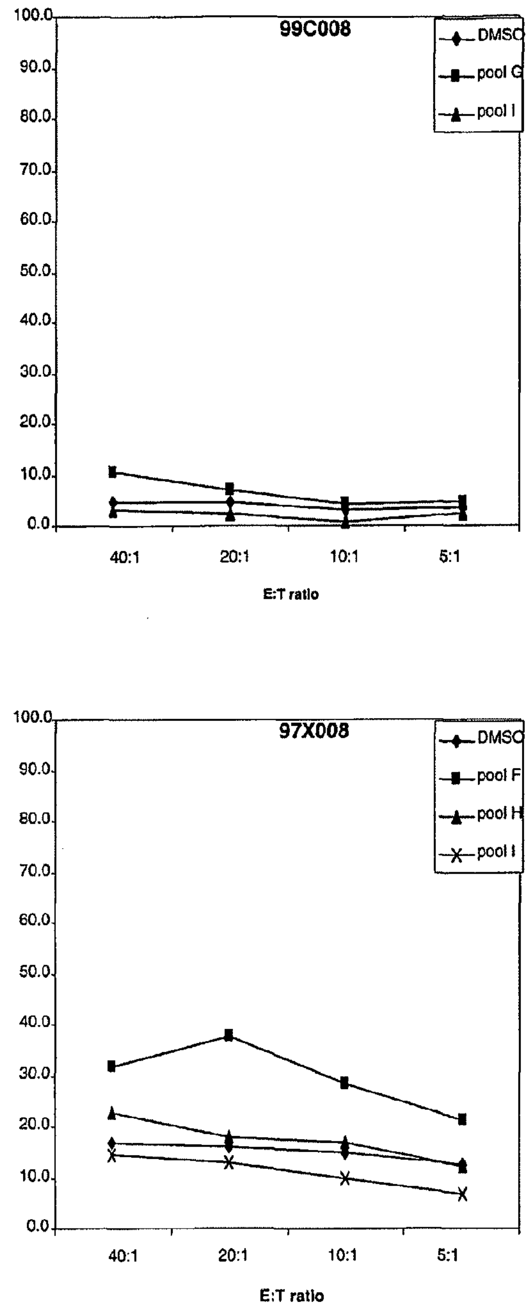
Pep pools	Ad5-NS 10^{11} vp/dose			
	99C008	*97N104*	*97X008*	*99C026*
F (NS3p)		1703	1136	615
G (NS3h)	3153			2787
H (NS4)				
I (NS5a)		2233		
L (NS5b)				
M (NS5b)				
DMSO	125	98	130	0

Pep pools	MRKAd6-NSmut 10^{11} vp/dose			
	98C047	*97C055*	*93G*	*97X014*
F (NS3p)	1024			948
G (NS3h)	3246	353		1074
H (NS4)			316	
I (NS5a)			6224	
L (NS5b)				
M (NS5b)				
DMSO	49	23	37	93

Pep pools	MRKAd5-NSmut 10^{11} vp/dose			
	99C059	*99C060*	*97X009*	*96069*
F (NS3p)			2266	5053
G (NS3h)	2434	316	1018	
H (NS4)				
I (NS5a)				
L (NS5b)				
M (NS5b)				205
DMSO	13	110	119	15

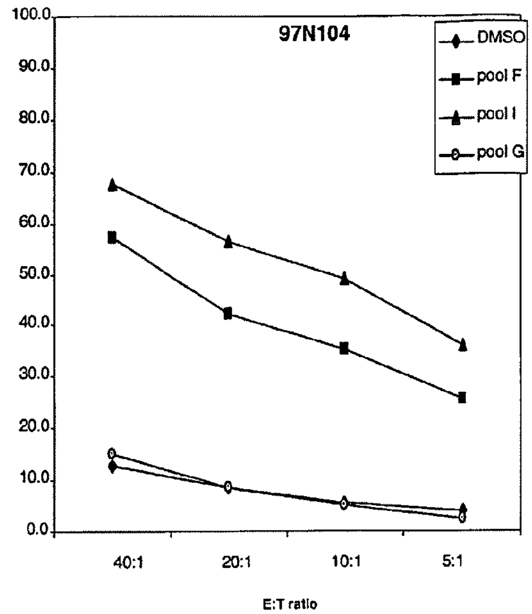
IFNγ ICS on PBMC from Rhesus monkeys immunized with two injections at four weeks interval with 10^{11} vp/dose of Adenovectors expressing the different HCV NS cassettes. Data are expressed as number of positive IFNγ/CD3/CD8 per 10^6 lymphocytes.

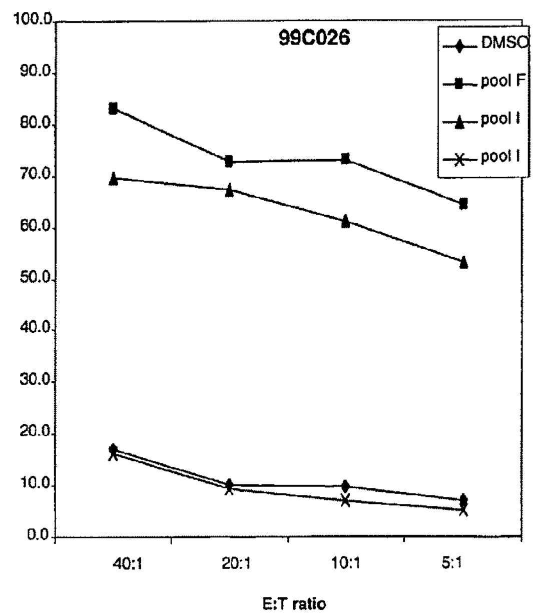
FIG. 17B



Bulk CTL assays on PBMC from Rhesus monkeys immunized with two injections of 10^{11}vp/dose of Ad5-NS.

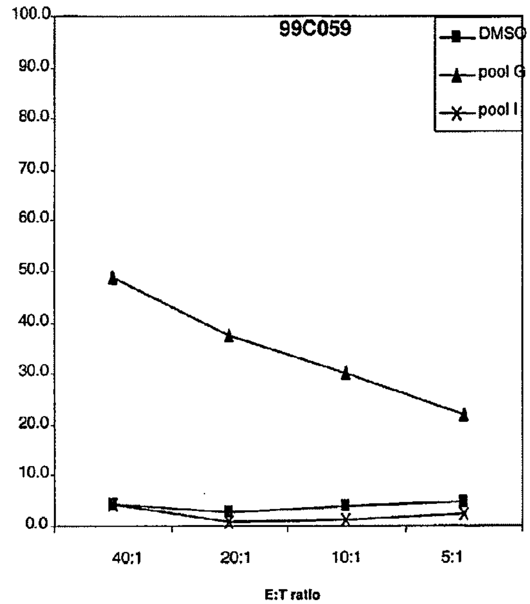
FIG. 18A

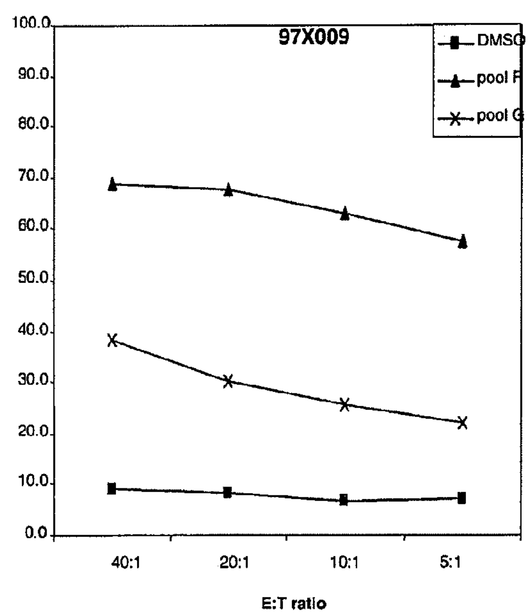




Bulk CTL assays on PBMC from Rhesus monkeys immunized with two injections of 10^{11}vp/dose of Ad5-NS.

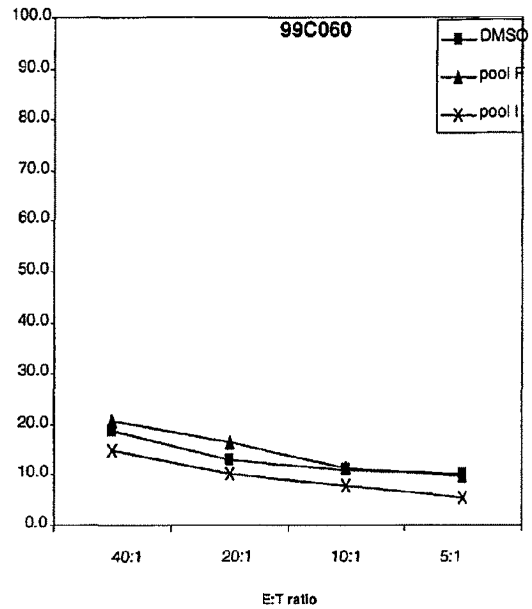
FIG. 18B

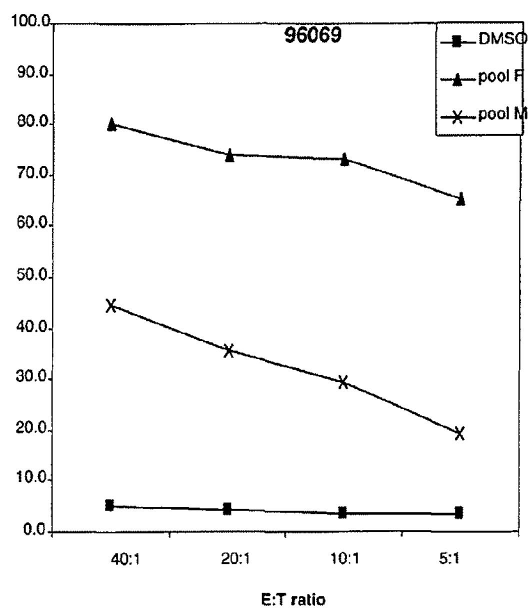




Bulk CTL assays on PBMC from Rhesus monkeys immunized with two injections of 10^{11}vp/dose of MRKAd5-NSmut.

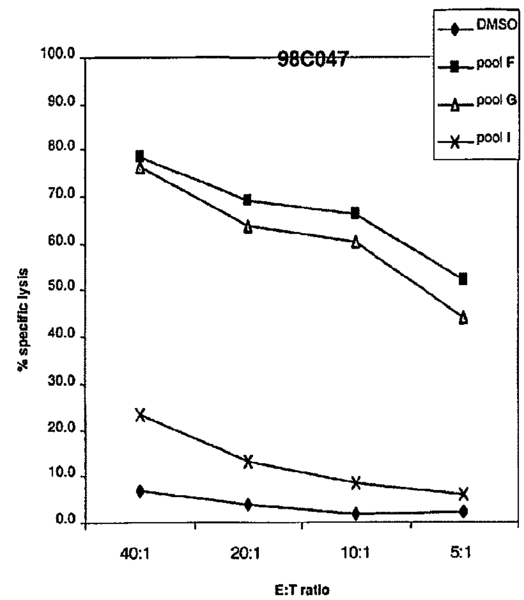
FIG. 18C

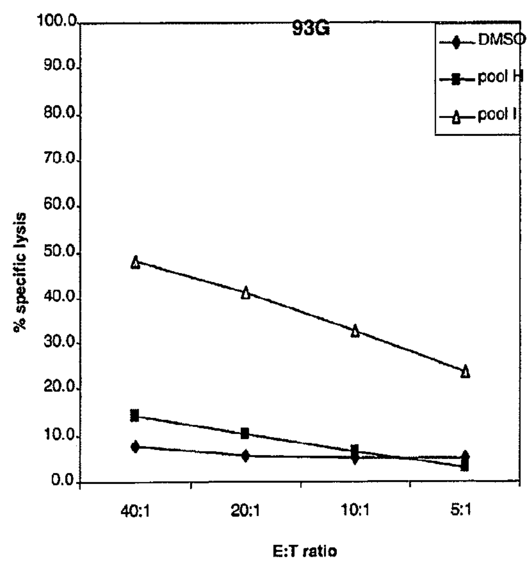




Bulk CTL assays on PBMC from Rhesus monkeys immunized with two injections of 10^{11}vp/dose of MRKAd5-NSmut

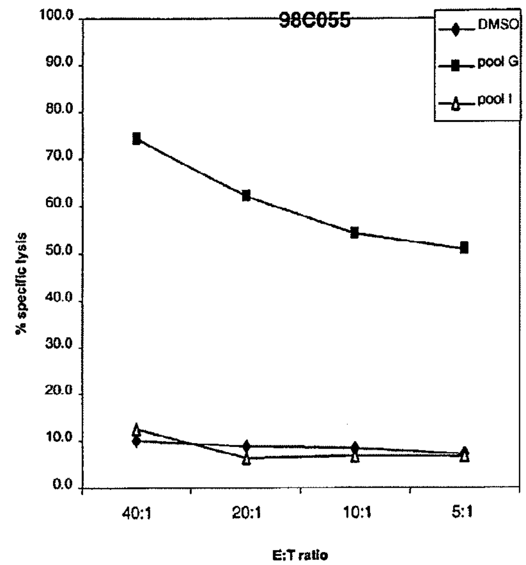
FIG. 18D

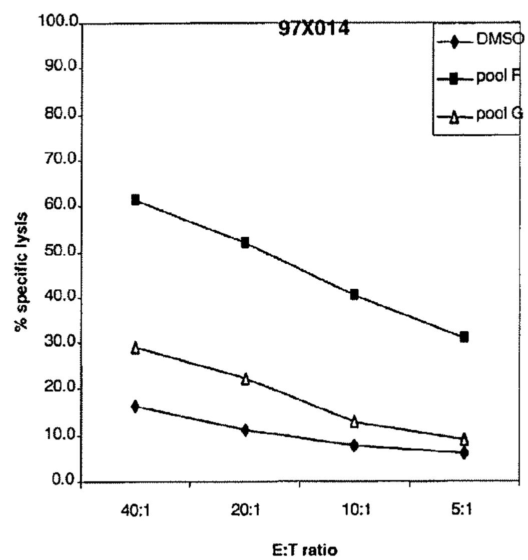




Bulk CTL assays on PBMC from Rhesus monkeys immunized with two injections of 10^{11}vp/dose of MRKAd6-NSmut.

FIG. 18E





Bulk CTL assays on PBMC from Rhesus monkeys immunized with two injections of 10^{11}vp/dose of MRKAd6-NSmut.

FIG. 18F

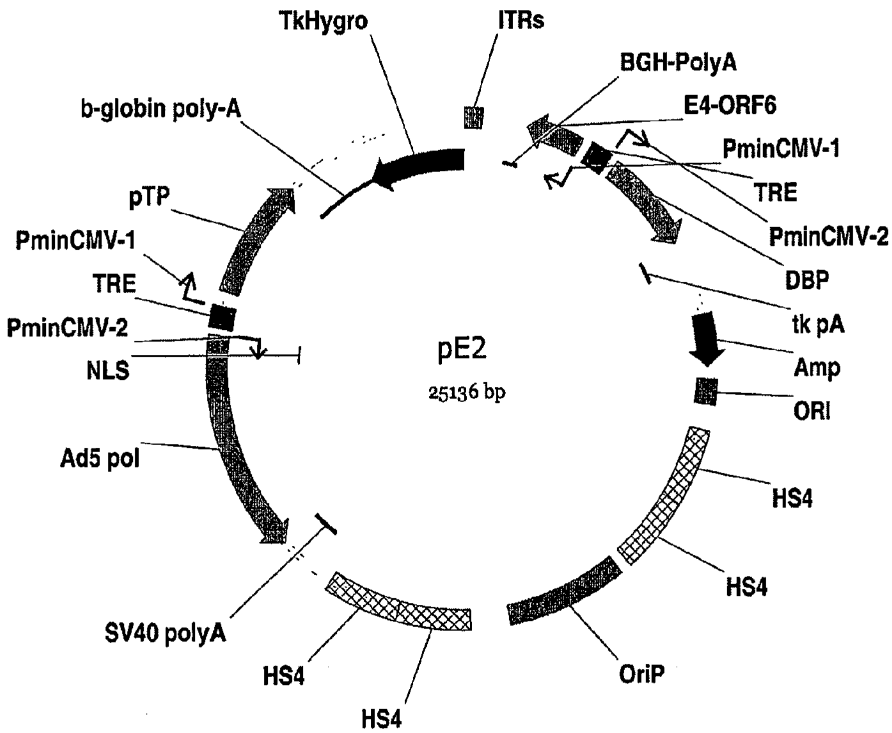

TkHygro
ITRs
BGH-PolyA
E4-ORF6
PminCMV-1
TRE
PminCMV-2
DBP
tk pA
Amp
ORI
HS4
HS4
OriP
HS4
HS4
SV40 polyA
Ad5 pol
NLS
PminCMV-2
TRE
PminCMV-1
pTP
b-globin poly-A
pE2
25136 bp

FIG. 19

1 GCCACCATGG CCCCCATCAC CGCCTACAGC CAGCAGACCA GGGGCCTGCT

51 GGGCTGCATC ATCACCAGCC TGACCGGACG CGACAAGAAC CAGGTGGAGG

101 GAGAGGTGCA GGTGGTGAGC ACCGCTACCC AGAGCTTCCT GGCCACCTGC

151 GTGAACGGCG TGTGCTGGAC CGTGTACCAC GGAGCCGGAA GCAAGACCCT

201 GGCCGGACCC AAGGGCCCTA TCACCCAGAT GTACACCAAT GTGGATCAGG

251 ATCTGGTGGG CTGGCAGGCC CCTCCCGGAG CCAGGAGCCT GACACCCTGT

301 ACCTGTGGAA GCAGCGACCT GTACCTGGTG ACACGCCACG CCGATGTGAT

351 CCCCGTGAGG CGCAGGGGCG ATTCTCGCGG AAGCCTGCTG AGCCCTAGGC

401 CCGTGAGCTA CCTGAAGGGC AGCAGCGGAG GACCCCTGCT GTGTCCTTCT

451 GGCCATGCCG TGGGCATTTT TCGCGCTGCC GTGTGTACCA GGGGCGTGGC

501 CAAAGCCGTG GATTTTGTGC CCGTGGAAAG CATGGAGACC ACCATGCGCA

551 GCCCTGTGTT CACCGACAAC AGCTCTCCCC CTGCCGTGCC CCAATCATTC

601 CAGGTGGCTC ACCTGCACGC CCCTACCGGA TCTGGCAAGA GCACCAAGGT

651 GCCCGCTGCC TACGCCGCTC AGGGCTACAA GGTGCTGGTG CTGAACCCCA

701 GCGTGGCCGC TACCCTGGGC TTCGGCGCTT ACATGAGCAA GGCCCATGGC

751 ATCGACCCCA ACATCCGCAC AGGCGTGCGC ACCATCACCA CCGGAGCTCC

801 CGTGACCTAC AGCACCTACG GCAAGTTCCT GGCCGATGGA GGCTGCAGCG

851 GAGGAGCCTA CGACATCATC ATCTGCGACG AGTGCCACAG CACCGACAGC

901 ACCACCATCC TGGGCATTGG CACCGTGCTG GATCAGGCCG AAACAGCTGG

951 AGCCAGGCTG GTGGTGCTGG CCACAGCTAC CCCTCCTGGC AGCGTGACCG

1001 TGCCCCATCC CAATATCGAG GAGGTGGCCC TGAGCAACAC AGGCGAGATC

1051 CCCTTCTACG GCAAGGCCAT CCCCATCGAG GCCATCCGCG GAGGCAGGCA

1101 CCTGATCTTC TGCCACAGCA AGAAGAAGTG CGACGAGCTG GCTGCCAAGC

1151 TGAGCGGACT GGGCATCAAC GCCGTGGCCT ACTACAGGGG CCTGGACGTG

1201 TCAGTGATCC CCACCATCGG CGATGTGGTG GTGGTGGCCA CCGACGCCCT

1251 GATGACAGGC TACACCGGAG ACTTCGACAG CGTGATCGAC TGCAACACCT

1301 GCGTGACCCA GACCGTGGAC TTCAGCCTGG ACCCCACCTT CACCATCGAA

1351 ACCACCACCG TGCCTCAGGA TGCTGTGAGC AGGAGCCAGA GGCGCGGACG

1401 CACCGGAAGG GGCAGGCGCG GAATTTATCG CTTTGTGACC CCTGGCGAAA

1451 GGCCCTCTGG CATGTTCGAC AGCAGCGTGC TGTGCGAGTG CTACGACGCT

1501 GGCTGCGCTT GGTACGAGCT GACACCCGCT GAAACCAGCG TGCGCCTGCG

1551 CGCTTATCTG AATACCCCTG GCCTGCCCGT GTGTCAGGAC CACCTGGAGT

FIG. 20A

1601 TCTGGGAGAG CGTGTTCACA GGACTGACCC ACATCGACGC CCATTTCCTG
1651 AGCCAGACCA AGCAGGCTGG CGACAACTTC CCCTATCTGG TGGCCTATCA
1701 GGCCACCGTG TGTGCTAGGG CCCAAGCTCC ACCTCCTTCA TGGGACCAGA
1751 TGTGGAAGTG CCTGATCCGC CTGAAGCCCA CCCTGCACGG CCCTACCCCT
1801 CTGCTGTACC GCCTGGGAGC CGTGCAGAAC GAGGTGACCC TGACCCACCC
1851 CATCACCAAG TACATCATGG CCTGCATGAG CGCTGATCTG GAAGTGGTGA
1901 CCAGCACCTG GGTGCTGGTG GGAGGCGTGC TGGCCGCTCT GGCTGCCTAC
1951 TGCCTGACCA CCGGAAGCGT GGTGATCGTG GGACGCATCA TCCTGAGCGG
2001 AAGGCCCGCT ATCGTGCCCG ATCGCGAGTT CCTGTACCAG GAGTTCGACG
2051 AGATGGAGGA GTGTGCCAGC CACCTGCCCT ACATCGAGCA GGGCATGCAG
2101 CTGGCCGAAC AGTTCAAGCA GAAGGCCCTG GGCCTGCTGC AGACAGCCAC
2151 CAAACAGGCC GAAGCTGCCG CTCCCGTGGT GGAAAGCAAG TGGAGGGCCC
2201 TGGAGACCTT CTGGGCTAAG CACATGTGGA ACTTCATCTC TGGCATCCAG
2251 TACCTGGCCG GACTGAGCAC CCTGCCTGGC AACCCCGCTA TCGCCAGCCT
2301 GATGGCCTTC ACCGCTAGCA TCACCTCTCC CCTGACCACC CAGAGCACCC
2351 TGCTGTTCAA CATTCTGGGC GGATGGGTGG CCGCTCAGCT GGCCCCTCCT
2401 TCAGCTGCTT CTGCCTTTGT GGGCGCTGGC ATTGCCGGAG CCGCTGTGGG
2451 CAGCATTGGC CTGGGCAAAG TGCTGGTGGA TATTCTGGCT GGCTATGGCG
2501 CTGGCGTGGC CGGAGCCCTG GTGGCCTTCA AGGTGATGAG CGGAGAGATG
2551 CCCAGCACCG AGGACCTGGT GAACCTGCTG CCTGCCATTC TGAGCCCTGG
2601 AGCCCTGGTG GTGGGCGTGG TGTGTGCTGC CATTCTGAGG CGCCATGTGG
2651 GACCCGGAGA GGGCGCTGTG CAGTGGATGA ACCGCCTGAT CGCCTTCGCC
2701 TCTCGCGGAA ACCACGTGAG CCCTACCCAC TACGTGCCTG AGAGCGACGC
2751 CGCTGCCAGG GTGACCCAGA TCCTGAGCAG CCTGACCATC ACCCAGCTGC
2801 TGAAGCGCCT GCACCAGTGG ATCAACGAGG ACTGCAGCAC ACCCTGCAGC
2851 GGAAGCTGGC TGAGGGACGT GTGGGACTGG ATCTGCACCG TGCTGACCGA
2901 CTTCAAGACC TGGCTGCAGA GCAAGCTGCT GCCCCAACTG CCTGGCGTGC
2951 CCTTCTTCTC ATGCCAGCGC GGATACAAGG GCGTGTGGAG GGGCGATGGC
3001 ATCATGCAGA CCACCTGTCC CTGCGGAGCC CAGATCACAG GCCACGTGAA
3051 GAACGGCAGC ATGCGCATCG TGGGCCCTAA GACCTGCAGC AACACCTGGC
3101 ACGGCACCTT CCCCATCAAC GCCTACACCA CCGGACCCTG CACACCCAGC
3151 CCTGCTCCCA ACTACAGCAG GGCCCTGTGG AGGGTGGCTG CCGAGGAGTA

FIG. 20B

3201 CGTGGAGGTG ACCAGGGTGG GAGACTTCCA CTACGTGACC GGAATGACCA
3251 CCGACAACGT GAAGTGTCCC TGTCAGGTGC CCGCTCCCGA ATTTTTTACC
3301 GAAGTGGATG GCGTGCGCCT GCATCGCTAT GCCCCTGCCT GTAGGCCCCT
3351 GCTGCGCGAA GAAGTGACCT TCCAGGTGGG CCTGAACCAG TACCTGGTGG
3401 GCAGCCAGCT GCCCTGCGAG CCTGAGCCCG ATGTGGCCGT GCTGACCAGC
3451 ATGCTGACCG ACCCCAGCCA CATCACAGCC GAAACCGCTA AAAGGCGCCT
3501 GGCCAGGGGC TCTCCTCCAA GCCTGGCCTC AAGCAGCGCT AGCCAGCTGT
3551 CTGCTCCCAG CCTGAAGGCC ACCTGCACCA CCCACCACGT GAGCCCCGAC
3601 GCCGACCTGA TCGAGGCCAA CCTGCTGTGG CGCCAGGAGA TGGGCGGCAA
3651 CATCACCCGC GTGGAGAGCG AGAACAAGGT GGTGGTGCTG GACAGCTTCG
3701 ACCCCCTGCG CGCCGAGGAG GACGAGCGCG AGGTGAGCGT GCCCGCCGAG
3751 ATCCTGCGCA AGAGCAAGAA GTTCCCCGCT GCCATGCCCA TCTGGGCTAG
3801 ACCTGATTAC AACCCTCCCC TGCTGGAGAG CTGGAAGGAC CCTGATTACG
3851 TGCCTCCAGT GGTGCATGGC TGTCCTCTGC CTCCCATTAA AGCCCCTCCT
3901 ATTCCACCTC CTAGGCGCAA AAGGACCGTG GTGCTGACAG AAAGCAGCGT
3951 GAGCTCTGCT CTGGCCGAAC TGGCCACCAA GACCTTTGGC AGCAGCGAGA
4001 GCTCTGCCGT GGACAGCGGA ACAGCCACCG CTCTGCCTGA CCAGGCCAGC
4051 GACGACGGCG ATAAGGGCAG CGATGTGGAG AGCTATAGCA GCATGCCTCC
4101 CCTGGAAGGC GAACCTGGCG ATCCCGATCT GAGCGATGGC AGCTGGAGCA
4151 CCGTGAGCGA AGAGGCCAGC GAGGACGTGG TGTGTTGCAG CATGAGCTAC
4201 ACCTGGACAG GCGCTCTGAT CACACCCTGC GCTGCCGAGG AGAGCAAGCT
4251 GCCCATCAAC GCCCTGAGCA ACAGCCTGCT GAGGCACCAC AACATGGTGT
4301 ACGCCACCAC CAGCAGGTCT GCCGGACTGA GGCAGAAGAA GGTGACCTTC
4351 GACCGCCTGC AGGTGCTGGA CGACCACTAC CGCGATGTGC TGAAGGAGAT
4401 GAAGGCCAAG GCCAGCACCG TGAAGGCCAA GCTGCTGAGC GTGGAGGAGG
4451 CCTGCAAGCT GACCCCCCCC CACAGCGCCA AGAGCAAGTT CGGCTACGGC
4501 GCCAAGGACG TGCGCAACCT GAGCAGCAAG GCCGTGAACC ACATCCACAG
4551 CGTGTGGAAG GACCTGCTGG AGGACACCGT GACCCCCATC GACACCACCA
4601 TCATGGCCAA GAACGAGGTG TTCTGCGTGC AGCCCGAGAA GGGCGGCCGC
4651 AAGCCCGCTC GCCTGATCGT GTTCCCCGAT CTGGGCGTGC GCGTGTGCGA
4701 GAAGATGGCC CTGTACGACG TGGTGAGCAC CCTGCCTCAG GTGGTGATGG
4751 GCTCAAGCTA CGGCTTCCAG TACAGCCCTG GCCAGCGCGT GGAGTTCCTG

FIG. 20C

4801 GTGAACACCT GGAAGAGCAA GAAGAACCCC ATGGGCTTCA GCTACGACAC
4851 ACGCTGCTTC GACAGCACCG TGACCGAGAA CGACATCCGC GTGGAGGAGA
4901 GCATCTACCA GTGCTGCGAC CTGGCCCCTG AGGCCAGGCA GGCCATCAAG
4951 AGCCTGACCG AGCGCCTGTA CATCGGAGGC CCTCTGACCA ACAGCAAGGG
5001 ACAGAACTGC GGATACAGGC GCTGTAGGGC CTCTGGCGTG CTGACCACCA
5051 GCTGTGGCAA CACCCTGACC TGCTACCTGA AGGCCAGCGC TGCCTGTCGC
5101 GCTGCCAAGC TGCAGGACTG CACCATGCTG GTGAACGCCG CTGGCCTGGT
5151 GGTGATTTGT GAAAGCGCTG GCACCCAGGA AGATGCTGCC AGCCTGCGCG
5201 TGTTCACCGA GGCCATGACC AGGTACTCTG CCCCTCCCGG AGACCCCCCT
5251 CAGCCCGAAT ACGACCTGGA GCTGATCACC AGCTGCTCAA GCAACGTGAG
5301 CGTGGCTCAC GACGCCAGCG GAAAGCGCGT GTACTACCTG ACACGCGATC
5351 CCACCACCCC TCTGGCTCGC GCTGCCTGGG AAACCGCTCG CCATACACCC
5401 GTGAACAGCT GGCTGGGCAA CATCATCATG TACGCCCCTA CCCTGTGGGC
5451 TCGCATGATC CTGATGACCC ACTTCTTCAG CATCCTGCTG GCTCAGGAGC
5501 AGCTGGAGAA GGCCCTGGAC TGCCAGATTT ACGGCGCTTG CTACAGCATC
5551 GAGCCCCTGG ACCTGCCCCA AATCATCGAG CGCCTGCACG GCCTGTCTGC
5601 CTTCAGCCTG CACAGCTACA GCCCTGGCGA AATTAATCGC GTGGCCAGCT
5651 GTCTGCGCAA ACTGGGCGTG CCTCCTCTGC GCGTGTGGAG GCATAGGGCT
5701 AGGAGCGTGA GGGCTAGGCT GCTGAGCCAG GGAGGCAGGG CCGCTACCTG
5751 TGGAAAGTAC CTGTTCAACT GGGCCGTGAA GACCAAGCTG AAGCTGACCC
5801 CTATCCCTGC CGCTAGCCAG CTGGACCTGA GCGGATGGTT CGTGGCTGGC
5851 TACAGCGGAG GCGACATCTA CCACAGCCTG TCTCGCGCTC GCCCTCGCTG
5901 GTTCATGCTG TGCCTGCTGC TGCTGAGCGT GGGCGTGGGC ATCTACCTGC
5951 TGCCCAACCG CTAAA

FIG. 20D

IN THE PCT RECEIVING OFFICE
OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Merck & Co., Inc		
PCT Serial No.:	To Be Assigned	Case No.: PCT ITR0015Y	US/RO
Filing date:	On Even Date Herewith		Authorized Officer: To Be Assigned
For:	HEPATITIS C VIRUS VACCINE		

Assistant Commissioner of Patents
BOX PCT
Washington, D.C. 20231

NUCLEOTIDE AND/OR AMINO ACID
SEQUENCE DISCLOSURE, PCT RULE 5.2

Sir:

As required under PCT Rule 5.2, Applicant respectfully encloses a paper (64 pages) and a computer readable form of the Sequence Listing for the above-identified PCT International Application, filed on even date herewith.

I hereby state that the content of the paper and computer readable forms of the Sequence Listing, submitted in accordance with WIPO and Standard ST.23 and under PCT Rule 13ter.1, respectively, are the same.

Respectfully submitted,

By [signature]

Sheldon O. Heber
Reg. No. 38,179
Attorney for Applicants

Merck & Co., Inc.
P.O. Box 2000
Rahway, NJ 07065-0907
(732) 594-1958

SEQUENCE LISTING

```
<110> Merck & Co. Inc., and Istituto Di Ricerche Di Biologia Molecolare P.
      Angeletti S.P.A.

<120> HEPATITIS C VIRUS VACCINE

<130> ITR0015Y

<150> 60/363,774
<151> 2002-03-13

<150> 60/328,655
<151> 2001-10-11

<160> 17

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 1985
<212> PRT
<213> Artificial Sequence

<220>
<223> Met-NS3-NS4A-NS4B-NS5A-NS5B polypeptide

<400> 1
Met Ala Pro Ile Thr Ala Tyr Ser Gln Gln Thr Arg Gly Leu Leu Gly
 1               5                   10                  15
Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
            20                  25                  30
Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
        35                  40                  45
Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
    50                  55                  60
Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
65                  70                  75                  80
Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
                85                  90                  95
Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
            100                 105                 110
Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
        115                 120                 125
Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
    130                 135                 140
Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
145                 150                 155                 160
Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
                165                 170                 175
Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
            180                 185                 190
Ala Val Pro Gln Ser Phe Gln Val Ala His Leu His Ala Pro Thr Gly
        195                 200                 205
```

```
Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
    210                 215                 220
Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
225                 230                 235                 240
Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
                245                 250                 255
Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
            260                 265                 270
Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
        275                 280                 285
Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
    290                 295                 300
Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
305                 310                 315                 320
Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
                325                 330                 335
Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
            340                 345                 350
Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
        355                 360                 365
Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
    370                 375                 380
Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
385                 390                 395                 400
Ile Pro Thr Ile Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met
                405                 410                 415
Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys
            420                 425                 430
Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu
        435                 440                 445
Thr Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly
    450                 455                 460
Arg Thr Gly Arg Gly Arg Arg Gly Ile Tyr Arg Phe Val Thr Pro Gly
465                 470                 475                 480
Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr
                485                 490                 495
Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Ser Val
            500                 505                 510
Arg Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln Asp
        515                 520                 525
His Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp
    530                 535                 540
Ala His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr
545                 550                 555                 560
Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro
                565                 570                 575
Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr
            580                 585                 590
Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn
        595                 600                 605
Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met
    610                 615                 620
Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly
625                 630                 635                 640
```

```
Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val Val
                645                 650                 655
Ile Val Gly Arg Ile Ile Leu Ser Gly Arg Pro Ala Ile Val Pro Asp
            660                 665                 670
Arg Glu Phe Leu Tyr Gln Glu Phe Asp Glu Met Glu Glu Cys Ala Ser
        675                 680                 685
His Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe Lys
    690                 695                 700
Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu Ala
705                 710                 715                 720
Ala Ala Pro Val Val Glu Ser Lys Trp Arg Ala Leu Glu Thr Phe Trp
                725                 730                 735
Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly
            740                 745                 750
Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe
        755                 760                 765
Thr Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Ser Thr Leu Leu Phe
    770                 775                 780
Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser Ala
785                 790                 795                 800
Ala Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Val Gly Ser
                805                 810                 815
Ile Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly Ala
            820                 825                 830
Gly Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu Met
        835                 840                 845
Pro Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro
    850                 855                 860
Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His
865                 870                 875                 880
Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala
                885                 890                 895
Phe Ala Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu
            900                 905                 910
Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr Ile
        915                 920                 925
Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys Ser
    930                 935                 940
Thr Pro Cys Ser Gly Ser Trp Leu Arg Asp Val Trp Asp Trp Ile Cys
945                 950                 955                 960
Thr Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu Pro
                965                 970                 975
Gln Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys Gly
            980                 985                 990
Val Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly Ala
        995                 1000                1005
Gln Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly Pro
    1010                1015                1020
Lys Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala Tyr
1025                1030                1035                1040
Thr Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg Ala
                1045                1050                1055
Leu Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Val Thr Arg Val Gly
            1060                1065                1070
```

```
Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys Pro
        1075                1080                1085
Cys Gln Val Pro Ala Pro Glu Phe Phe Thr Glu Val Asp Gly Val Arg
    1090                1095                1100
Leu His Arg Tyr Ala Pro Ala Cys Arg Pro Leu Leu Arg Glu Glu Val
1105                1110                1115                1120
Thr Phe Gln Val Gly Leu Asn Gln Tyr Leu Val Gly Ser Gln Leu Pro
                1125                1130                1135
Cys Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp
            1140                1145                1150
Pro Ser His Ile Thr Ala Glu Thr Ala Lys Arg Arg Leu Ala Arg Gly
        1155                1160                1165
Ser Pro Pro Ser Leu Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro
    1170                1175                1180
Ser Leu Lys Ala Thr Cys Thr Thr His His Val Ser Pro Asp Ala Asp
1185                1190                1195                1200
Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile
                1205                1210                1215
Thr Arg Val Glu Ser Glu Asn Lys Val Val Val Leu Asp Ser Phe Asp
            1220                1225                1230
Pro Leu Arg Ala Glu Glu Asp Glu Arg Glu Val Ser Val Pro Ala Glu
        1235                1240                1245
Ile Leu Arg Lys Ser Lys Lys Phe Pro Ala Ala Met Pro Ile Trp Ala
    1250                1255                1260
Arg Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp
1265                1270                1275                1280
Tyr Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala
                1285                1290                1295
Pro Pro Ile Pro Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu
            1300                1305                1310
Ser Ser Val Ser Ser Ala Leu Ala Glu Leu Ala Thr Lys Thr Phe Gly
        1315                1320                1325
Ser Ser Glu Ser Ser Ala Val Asp Ser Gly Thr Ala Thr Ala Leu Pro
    1330                1335                1340
Asp Gln Ala Ser Asp Asp Gly Asp Lys Gly Ser Asp Val Glu Ser Tyr
1345                1350                1355                1360
Ser Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser
                1365                1370                1375
Asp Gly Ser Trp Ser Thr Val Ser Glu Glu Ala Ser Glu Asp Val Val
            1380                1385                1390
Cys Cys Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr Pro Cys
        1395                1400                1405
Ala Ala Glu Glu Ser Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu
    1410                1415                1420
Leu Arg His His Asn Met Val Tyr Ala Thr Thr Ser Arg Ser Ala Gly
1425                1430                1435                1440
Leu Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Asp
                1445                1450                1455
His Tyr Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser Thr Val
            1460                1465                1470
Lys Ala Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr Pro Pro
        1475                1480                1485
His Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Asn
    1490                1495                1500
```

Leu Ser Ser Lys Ala Val Asn His Ile His Ser Val Trp Lys Asp Leu
1505 1510 1515 1520
Leu Glu Asp Thr Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn
1525 1530 1535
Glu Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg
1540 1545 1550
Leu Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala
1555 1560 1565
Leu Tyr Asp Val Val Ser Thr Leu Pro Gln Val Val Met Gly Ser Ser
1570 1575 1580
Tyr Gly Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn
1585 1590 1595 1600
Thr Trp Lys Ser Lys Lys Asn Pro Met Gly Phe Ser Tyr Asp Thr Arg
1605 1610 1615
Cys Phe Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser
1620 1625 1630
Ile Tyr Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys
1635 1640 1645
Ser Leu Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys
1650 1655 1660
Gly Gln Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr
1665 1670 1675 1680
Thr Ser Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala
1685 1690 1695
Cys Arg Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Ala Ala
1700 1705 1710
Gly Leu Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala
1715 1720 1725
Ser Leu Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro
1730 1735 1740
Gly Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys
1745 1750 1755 1760
Ser Ser Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr
1765 1770 1775
Tyr Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu
1780 1785 1790
Thr Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met
1795 1800 1805
Tyr Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe
1810 1815 1820
Ser Ile Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln
1825 1830 1835 1840
Ile Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile
1845 1850 1855
Ile Glu Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser
1860 1865 1870
Pro Gly Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val
1875 1880 1885
Pro Pro Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg
1890 1895 1900
Leu Leu Ser Gln Gly Gly Arg Ala Ala Thr Cys Gly Lys Tyr Leu Phe
1905 1910 1915 1920
Asn Trp Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Ile Pro Ala Ala
1925 1930 1935

Ser Gln Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Ser Gly Gly
1940 1945 1950
Asp Ile Tyr His Ser Leu Ser Arg Ala Arg Pro Arg Trp Phe Met Leu
1955 1960 1965
Cys Leu Leu Leu Leu Ser Val Gly Val Gly Ile Tyr Leu Leu Pro Asn
1970 1975 1980
Arg
1985

<210> 2
<211> 5965
<212> DNA
<213> Artificial Sequence

<220>
<223> Non-optimized cDNA sequence encoding SEQ. ID. NO. 1

<400> 2
gccaccatgg cgcccatcac ggcctactcc caacagacgc ggggcctact tggttgcatc 60
atcactagcc ttacaggccg ggacaagaac caggtcgagg gagaggttca ggtggtttcc 120
accgcaacac aatccttcct ggcgacctgc gtcaacggcg tgtgttggac cgtttaccat 180
ggtgctggct caaagacctt agccggccca aaggggccaa tcacccagat gtacactaat 240
gtggaccagg acctcgtcgg ctggcaggcg ccccccgggg cgcgttcctt gacaccatgc 300
acctgtggca gctcagacct ttacttggtc acgagacatg ctgacgtcat tccggtgcgc 360
cggcggggcg acagtagggg gagcctgctc tcccccaggc ctgtctccta cttgaagggc 420
tcttcgggtg gtccactgct ctgcccttcg gggcacgctg tgggcatctt ccgggctgcc 480
gtatgcaccc ggggggttgc gaaggcggtg gactttgtgc ccgtagagtc catggaaact 540
actatgcggt ctccggtctt cacggacaac tcatcccccc cggccgtacc gcagtcattt 600
caagtggccc acctacacgc tcccactggc agcggcaaga gtactaaagt gccggctgca 660
tatgcagccc aagggtacaa ggtgctcgtc ctcaatccgt ccgttgccgc taccttaggg 720
tttggggcgt atatgtctaa ggcacacggt attgacccca acatcagaac tggggtaagg 780
accattacca caggcgcccc cgtcacatac tctacctatg gcaagtttct tgccgatggt 840
ggttgctctg gggcgcttta tgacatcata atatgtgatg agtgccattc aactgactcg 900
actacaatct tgggcatcgg cacagtcctg gaccaagcgg agacggctgg agcgcggctt 960
gtcgtgctcg ccaccgctac gcctccggga tcggtcaccg tgccacaccc aaacatcgag 1020
gaggtggccc tgtctaatac tggagagatc cccttctatg gcaaagccat ccccattgaa 1080
gccatcaggg gggggaaggca tctcatttc tgtcattcca agaagaagtg cgacgagctc 1140
gccgcaaagc tgtcaggcct cggaatcaac gctgtggcgt attaccgggg gctcgatgtg 1200
tccgtcatac caactatcgg agacgtcgtt gtcgtggcaa cagacgctct gatgacgggc 1260
tatacgggcg actttgactc agtgatcgac tgtaacacat gtgtcaccca gacagtcgac 1320
ttcagcttgg atcccacctt caccattgag acgacgaccg tgcctcaaga cgcagtgtcg 1380
cgctcgcagc ggcggggtag gactggcagg ggtaggagag gcatctacag gtttgtgact 1440
ccgggagaac ggccctcggg catgttcgat tcctcggtcc tgtgtgagtg ctatgacgcg 1500
ggctgtgctt ggtacgagct cacccccgcc gagacctcgg ttaggttgcg ggcctacctg 1560
aacacaccag ggttgcccgt ttgccaggac cacctggagt tctgggagag tgtcttcaca 1620
ggcctcaccc acatagatgc acacttcttg tcccagacca agcaggcagg agacaacttc 1680
ccctacctgg tagcatacca agccacggtg tgcgccaggg ctcaggcccc acctccatca 1740
tgggatcaaa tgtggaagtg tctcatacgg ctgaaaccta cgctgcacgg gccaacaccc 1800
ttgctgtaca ggctgggagc cgtccaaaat gaggtcaccc tcacccaccc cataaccaaa 1860
tacatcatgg catgcatgtc ggctgacctg gaggtcgtca ctagcacctg ggtgctggtg 1920
ggcggagtcc ttgcagctct ggccgcgtat tgcctgacaa caggcagtgt ggtcattgtg 1980
ggtaggatta tcttgtccgg gaggccggct attgttcccg acagggagtt tctctaccag 2040
gagttcgatg aaatggaaga gtgcgcctcg cacctcccct acatcgagca gggaatgcag 2100
ctcgccgagc aattcaagca gaaagcgctc gggttactgc aaacagccac caaacaagcg 2160

```
gaggctgctg ctcccgtggt ggagtccaag tggcgagccc ttgagacatt ctgggcgaag 2220
cacatgtgga atttcatcag cgggatacag tacttagcag gcttatccac tctgcctggg 2280
aaccccgcaa tagcatcatt gatggcattc acagcctcta tcaccagccc gctcaccacc 2340
caaagtaccc tcctgtttaa catcttgggg gggtgggtgg ctgcccaact cgcccccccc 2400
agcgccgctt cggctttcgt gggcgccggc atcgccggtg cggctgttgg cagcataggc 2460
cttgggaagg tgcttgtgga cattctggcg ggttatggag caggagtggc cggcgcgctc 2520
gtggccttca aggtcatgag cggcgagatg ccctccaccg aggacctggt caatctactt 2580
cctgccatcc tctctcctgg cgccctggtc gtcggggtcg tgtgtgcagc aatactgcgt 2640
cgacacgtgg gtccgggaga gggggctgtg cagtggatga accggctgat agcgttcgcc 2700
tcgcggggta atcatgtttc ccccacgcac tatgtgcctg agagcgacgc cgcagcgcgt 2760
gttactcaga tcctctccag ccttaccatc actcagctgc tgaaaaggct ccaccagtgg 2820
attaatgaag actgctccac accgtgttcc ggctcgtggc taagggatgt ttgggactgg 2880
atatgcacgg tgttgactga cttcaagacc tggctccagt ccaagctcct gccgcagcta 2940
ccgggagtcc ctttttctc gtgccaacgc gggtacaagg gagtctggcg gggagacggc 3000
atcatgcaaa ccacctgccc atgtggagca cagatcaccg gacatgtcaa aaacggttcc 3060
atgaggatcg tcgggcctaa gacctgcagc aacacgtggc atggaacatt ccccatcaac 3120
gcatacacca cgggccctg cacaccctct ccagcgccaa actattctag ggcgctgtgg 3180
cgggtggccg ctgaggagta cgtggaggtc acgcgggtgg gggatttcca ctacgtgacg 3240
ggcatgacca ctgacaacgt aaagtgccca tgccaggttc cggctcctga attcttcacg 3300
gaggtggacg gagtgcggtt gcacaggtac gctccggcgt gcaggcctct cctacgggag 3360
gaggttacat tccaggtcgg gctcaaccaa tacctggttg ggtcacagct accatgcgag 3420
cccgaaccgg atgtagcagt gctcacttcc atgctcaccg acccctccca catcacagca 3480
gaaacggcta agcgtaggtt ggccaggggg tctccccct ccttggccag ctcttcagct 3540
agccagttgt ctgcgccttc cttgaaggcg acatgcacta cccaccatgt ctctccggac 3600
gctgacctca tcgaggccaa cctcctgtgg cggcaggaga tgggcgggaa catcacccgc 3660
gtggagtcgg agaacaaggt ggtagtcctg gactctttcg acccgcttcg agcggaggag 3720
gatgagaggg aagtatccgt tccggcggag atcctgcgga aatccaagaa gttccccgca 3780
gcgatgccca tctgggcgcg cccggattac aaccctccac tgttagagtc ctggaaggac 3840
ccggactacg tccctccggt ggtgcacggg tgcccgttgc cacctatcaa ggcccctcca 3900
ataccacctc cacggagaaa gaggacggtt gtcctaacag agtcctccgt gtcttctgcc 3960
ttagcggagc tcgctactaa gaccttcggc agctccgaat catcggccgt cgacagcggc 4020
acggcgaccg cccttcctga ccaggcctcc gacgacggtg acaaaggatc cgacgttgag 4080
tcgtactcct ccatgccccc ccttgagggg gaaccggggg accccgatct cagtgacggg 4140
tcttggtcta ccgtgagcga ggaagctagt gaggatgtcg tctgctgctc aatgtcctac 4200
acatggacag gcgccttgat cacgccatgc gctgcggagg aaagcaagct gcccatcaac 4260
gcgttgagca actctttgct gcgccaccat aacatggttt atgccacaac atctcgcagc 4320
gcaggcctgc ggcagaagaa ggtcaccttt gacagactgc aagtcctgga cgaccactac 4380
cgggacgtgc tcaaggagat gaaggcgaag gcgtccacag ttaaggctaa actcctatcc 4440
gtagaggaag cctgcaagct gacgccccca cattcggcca aatccaagtt tggctatggg 4500
gcaaaggacg tccggaacct atccagcaag gccgttaacc acatccactc cgtgtggaag 4560
gacttgctgg aagacactgt gacaccaatt gacaccacca tcatggcaaa aaatgaggtt 4620
ttctgtgtcc aaccagagaa aggaggccgt aagccagccc gccttatcgt attcccagat 4680
ctgggagtcc gtgtatgcga gaagatggcc ctctatgatg tggtctccac ccttcctcag 4740
gtcgtgatgg gctcctcata cggattccag tactctcctg ggcagcgagt cgagttcctg 4800
gtgaatacct ggaaatcaaa gaaaaacccc atgggctttt catatgacac tcgctgtttc 4860
gactcaacgg tcaccgagaa cgacatccgt gttgaggagt caatttacca atgttgtgac 4920
ttggcccccg aagccagaca ggccataaaa tcgctcacag agcggcttta tatcgggggt 4980
cctctgacta attcaaaagg gcagaactgc ggttatcgcc ggtgccgcgc gagcggcgtg 5040
ctgacgacta gctgcggtaa caccctcaca tgttacttga aggcctctgc agcctgtcga 5100
gctgcgaagc tccaggactg cacgatgctc gtgaacgccg ccggccttgt cgttatctgt 5160
gaaagcgcgg gaacccaaga ggacgcggcg agcctacgag tcttcacgga ggctatgact 5220
aggtactctg ccccccccgg ggacccgccc caaccagaat acgacttgga gctgataaca 5280
tcatgttcct ccaatgtgtc ggtcgcccac gatgcatcag gcaaaagggt gtactacctc 5340
acccgtgatc ccaccacccc cctcgcacgg gctgcgtggg aaacagctag acacactcca 5400
gttaactcct ggctaggcaa cattatcatg tatgcgccca ctttgtgggc aaggatgatt 5460
```

ctgatgactc acttcttctc catccttcta gcacaggagc aacttgaaaa agccctggac 5520
tgccagatct acggggcctg ttactccatt gagccacttg acctacctca gatcattgaa 5580
cgactccatg gccttagcgc attttcactc catagttact ctccaggtga gatcaatagg 5640
gtggcttcat gcctcaggaa acttggggta ccacccttgc gagtctggag acatcgggcc 5700
aggagcgtcc gcgctaggct actgtcccag ggggggaggg ccgccacttg tggcaagtac 5760
ctcttcaact gggcagtgaa gaccaaactc aaactcactc caatcccggc tgcgtcccag 5820
ctggacttgt ccggctggtt cgttgctggt tacagcgggg gagacatata tcacagcctg 5880
tctcgtgccc gaccccgctg gttcatgctg tgcctactcc tactttctgt aggggtaggc 5940
atctacctgc tccccaaccg ataaa 5965

<210> 3
<211> 5965
<212> DNA
<213> Artificial Sequence

<220>
<223> Optimized cDNA encoding SEQ ID NO: 1

<400> 3
gccaccatgg cccccatcac cgcctacagc cagcagaccc gcggcctgct gggctgcatc 60
atcaccagcc tgaccggccg cgacaagaac caggtggagg gcgaggtgca ggtggtgagc 120
accgccaccc agagcttcct ggccacctgc gtgaacggcg tgtgctggac cgtgtaccac 180
ggcgccggca gcaagaccct ggccggcccc aagggcccca tcacccagat gtacaccaac 240
gtggaccagg acctggtggg ctggcaggcc ccccccggcg cccgcagcct gacccсctgc 300
acctgcggca gcagcgacct gtacctggtg acccgccacg ccgacgtgat ccccgtgcgc 360
cgccgcggcg acagccgcgg cagcctgctg agccccсgcc ccgtgagcta cctgaagggc 420
agcagcggcg gcccсctgct gtgccccagc ggccacgccg tgggcatctt ccgcgccgcc 480
gtgtgcaccc gcggcgtggc caaggccgtg gacttcgtgc ccgtggagag catggagacc 540
accatgcgca gccccgtgtt caccgacaac agcagccccc ccgccgtgcc ccagagcttc 600
caggtggccc acctgcacgc ccccaccggc agcggcaaga gcaccaaggt gcccgccgcc 660
tacgccgccc agggctacaa ggtgctggtg ctgaacccca gcgtggccgc caccctgggc 720
ttcggcgcct acatgagcaa ggcccacggc atcgacccca acatccgcac cggcgtgcgc 780
accatcacca ccggcgcccc cgtgacctac agcacctacg gcaagttcct ggccgacggc 840
ggctgcagcg gcggcgccta cgacatcatc atctgcgacg agtgccacag caccgacagc 900
accaccatcc tgggcatcgg caccgtgctg gaccaggccg agaccgccgg cgcccgcctg 960
gtggtgctgg ccaccgccac cccccccggc agcgtgaccg tgccccaccc caacatcgag 1020
gaggtggccc tgagcaacac cggcgagatc cccttctacg gcaaggccat ccccatcgag 1080
gccatccgcg gcggccgcca cctgatcttc tgccacagca agaagaagtg cgacgagctg 1140
gccgccaagc tgagcggcct gggcatcaac gccgtggcct actaccgcgg cctggacgtg 1200
agcgtgatcc ccaccatcgg cgacgtggtg gtggtggcca ccgacgccct gatgaccggc 1260
tacaccggcg acttcgacag cgtgatcgac tgcaacacct gcgtgaccca gaccgtggac 1320
ttcagcctgg accccacctt caccatcgag accaccaccg tgccccagga cgccgtgagc 1380
cgcagccagc gccgcggccg caccggccgc ggccgccgcg gcatctaccg cttcgtgacc 1440
cccggcgagc gccccagcgg catgttcgac agcagcgtgc tgtgcgagtg ctacgacgcc 1500
ggctgcgcct ggtacgagct gaccccсgcc gagaccagcg tgcgcctgcg cgcctacctg 1560
aacacccccg gcctgcccgt gtgccaggac cacctggagt tctgggagag cgtgttcacc 1620
ggcctgaccc acatcgacgc ccacttcctg agccagacca agcaggccgg cgacaacttc 1680
ccctacctgg tggcctacca ggccaccgtg tgcgcccgcg cccaggcccc cccccccagc 1740
tgggaccaga tgtggaagtg cctgatccgc ctgaagccca ccctgcacgg ccccacсccc 1800
ctgctgtacc gcctgggcgc cgtgcagaac gaggtgaccc tgacccaccc catcaccaag 1860
tacatcatgg cctgcatgag cgccgacctg gaggtggtga ccagcacctg ggtgctggtg 1920
ggcggcgtgc tggccgccct ggccgcctac tgcctgacca ccggcagcgt ggtgatcgtg 1980
ggccgcatca tcctgagcgg ccgccccgcc atcgtgcccg accgcgagtt cctgtaccag 2040
gagttcgacg agatggagga gtgcgccagc cacctgccct acatcgagca gggcatgcag 2100
ctggccgagc agttcaagca gaaggccctg ggcctgctgc agaccgccac caagcaggcc 2160

gaggccgccg cccccgtggt ggagagcaag tggcgcgccc tggagacctt ctgggccaag 2220
cacatgtgga acttcatcag cggcatccag tacctggccg gcctgagcac cctgcccggc 2280
aaccccgcca tcgccagcct gatggccttc accgccagca tcaccagccc cctgaccacc 2340
cagagcaccc tgctgttcaa catcctgggc ggctgggtgg ccgcccagct ggcccccccc 2400
agcgccgcca gcgccttcgt gggcgccggc atcgccggcg ccgccgtggg cagcatcggc 2460
ctgggcaagg tgctggtgga catcctggcc ggctacggcg ccggcgtggc cggcgccctg 2520
gtggccttca aggtgatgag cggcgagatg cccagcaccg aggacctggt gaacctgctg 2580
cccgccatcc tgagccccgg cgccctggtg gtgggcgtgg tgtgcgccgc catcctgcgc 2640
cgccacgtgg gccccggcga gggcgccgtg cagtggatga accgcctgat cgccttcgcc 2700
agccgcggca accacgtgag ccccacccac tacgtgcccg agagcgacgc cgccgcccgc 2760
gtgacccaga tcctgagcag cctgaccatc acccagctgc tgaagcgcct gcaccagtgg 2820
atcaacgagg actgcagcac cccctgcagc ggcagctggc tgcgcgacgt gtgggactgg 2880
atctgcaccg tgctgaccga cttcaagacc tggctgcaga gcaagctgct gccccagctg 2940
cccggcgtgc ccttcttcag ctgccagcgc ggctacaagg gcgtgtggcg cggcgacggc 3000
atcatgcaga ccacctgccc ctgcggcgcc cagatcaccg gccacgtgaa gaacggcagc 3060
atgcgcatcg tgggccccaa gacctgcagc aacacctggc acggcacctt ccccatcaac 3120
gcctacacca ccggcccctg cacccccagc cccgccccca actacagccg cgccctgtgg 3180
cgcgtggccg ccgaggagta cgtggaggtg acccgcgtgg gcgacttcca ctacgtgacc 3240
ggcatgacca ccgacaacgt gaagtgcccc tgccaggtgc ccgcccccga gttcttcacc 3300
gaggtggacg gcgtgcgcct gcaccgctac gcccccgcct gccgccccct gctgcgcgag 3360
gaggtgacct tccaggtggg cctgaaccag tacctggtgg gcagccagct gccctgcgag 3420
cccgagcccg acgtggccgt gctgaccagc atgctgaccg accccagcca catcaccgcc 3480
gagaccgcca agcgccgcct ggcccgcggc agcccccccа gcctggccag cagcagcgcc 3540
agccagctga gcgcccccag cctgaaggcc acctgcacca cccaccacgt gagccccgac 3600
gccgacctga tcgaggccaa cctgctgtgg cgccaggaga tgggcggcaa catcacccgc 3660
gtggagagcg agaacaaggt ggtggtgctg gacagcttcg acccccctgcg cgccgaggag 3720
gacgagcgcg aggtgagcgt gcccgccgag atcctgcgca agagcaagaa gttccccgcc 3780
gccatgccca tctgggcccg ccccgactac aacccccccc tgctggagag ctggaaggac 3840
cccgactacg tgccccccgt ggtgcacggc tgccccctgc cccccatcaa ggcccccccc 3900
atcccccccc cccgccgcaa gcgcaccgtg gtgctgaccg agagcagcgt gagcagcgcc 3960
ctggccgagc tggccaccaa gaccttcggc agcagcgaga gcagcgccgt ggacagcggc 4020
accgccaccg ccctgcccga ccaggccagc gacgacggcg acaagggcag cgacgtggag 4080
agctacagca gcatgccccc cctggagggc gagcccggcg accccgacct gagcgacggc 4140
agctggagca ccgtgagcga ggaggccagc gaggacgtgg tgtgctgcag catgagctac 4200
acctggaccg gcgccctgat caccccctgc gccgccgagg agagcaagct gcccatcaac 4260
gccctgagca acagcctgct gcgccaccac aacatggtgt acgccaccac cagccgcagc 4320
gccggcctgc gccagaagaa ggtgaccttc gaccgcctgc aggtgctgga cgaccactac 4380
cgcgacgtgc tgaaggagat gaaggccaag gccagcaccg tgaaggccaa gctgctgagc 4440
gtggaggagg cctgcaagct gacccccccc cacagcgcca agagcaagtt cggctacggc 4500
gccaaggacg tgcgcaacct gagcagcaag gccgtgaacc acatccacag cgtgtggaag 4560
gacctgctgg aggacaccgt gacccccatc gacaccacca tcatggccaa gaacgaggtg 4620
ttctgcgtgc agcccgagaa gggcggccgc aagcccgccc gcctgatcgt gttccccgac 4680
ctgggcgtgc gcgtgtgcga gaagatggcc ctgtacgacg tggtgagcac cctgccccag 4740
gtggtgatgg gcagcagcta cggcttccag tacagccccg gccagcgcgt ggagttcctg 4800
gtgaacacct ggaagagcaa gaagaacccc atgggcttca gctacgacac ccgctgcttc 4860
gacagcaccg tgaccgagaa cgacatccgc gtggaggaga gcatctacca gtgctgcgac 4920
ctggcccccg aggcccgcca ggccatcaag agcctgaccg agcgcctgta catcggcggc 4980
cccctgacca acagcaaggg ccagaactgc ggctaccgcc gctgccgcgc cagcggcgtg 5040
ctgaccacca gctgcggcaa caccctgacc tgctacctga aggccagcgc cgcctgccgc 5100
gccgccaagc tgcaggactg caccatgctg gtgaacgccg ccggcctggt ggtgatctgc 5160
gagagcgccg gcacccagga ggacgccgcc agcctgcgcg tgttcaccga ggccatgacc 5220
cgctacagcg ccccccccgg cgaccccccc cagcccgagt acgacctgga gctgatcacc 5280
agctgcagca gcaacgtgag cgtggcccac gacgccagcg gcaagcgcgt gtactacctg 5340
acccgcgacc ccaccacccc cctggcccgc gccgcctggg agaccgcccg ccacaccccc 5400
gtgaacagct ggctgggcaa catcatcatg tacgccccca ccctgtgggc ccgcatgatc 5460

ctgatgaccc acttcttcag catcctgctg gcccaggagc agctggagaa ggccctggac 5520
tgccagatct acggcgcctg ctacagcatc gagcccctgg acctgcccca gatcatcgag 5580
cgcctgcacg gcctgagcgc cttcagcctg cacagctaca gccccggcga gatcaaccgc 5640
gtggccagct gcctgcgcaa gctgggcgtg cccccctgc gcgtgtggcg ccaccgcgcc 5700
cgcagcgtgc gcgcccgcct gctgagccag ggcggccgcg ccgccacctg cggcaagtac 5760
ctgttcaact gggccgtgaa gaccaagctg aagctgaccc ccatccccgc cgccagccag 5820
ctggacctga gcggctggtt cgtggccggc tacagcggcg gcgacatcta ccacagcctg 5880
agccgcgccc gcccccgctg gttcatgctg tgcctgctgc tgctgagcgt gggcgtgggc 5940
atctacctgc tgcccaaccg ctaaa 5965

<210> 4
<211> 37090
<212> DNA
<213> Artificial Sequence

<220>
<223> MRKAd6-NSmut nucleic acid

<400> 4
catcatcaat aatatacctt attttggatt gaagccaata tgataatgag ggggtggagt 60
ttgtgacgtg gcgcggggcg tgggaacggg gcgggtgacg tagtagtgtg gcggaagtgt 120
gatgttgcaa gtgtggcgga acacatgtaa gcgacggatg tggcaaaagt gacgtttttg 180
gtgtgcgccg gtgtacacag gaagtgacaa ttttcgcgcg gttttaggcg gatgttgtag 240
taaatttggg cgtaaccgag taagatttgg ccattttcgc gggaaaactg aataagagga 300
agtgaaatct gaataatttt gtgttactca tagcgcgtaa tatttgtcta gggccgcggg 360
gactttgacc gtttacgtgg agactcgccc aggtgttttt ctcaggtgtt ttccgcgttc 420
cgggtcaaag ttggcgtttt attattatag gcggccgcga tccattgcat acgttgtatc 480
catatcataa tatgtacatt tatattggct catgtccaac attaccgcca tgttgacatt 540
gattattgac tagttattaa tagtaatcaa ttacggggtc attagttcat agcccatata 600
tggagttccg cgttacataa cttacggtaa atggcccgcc tggctgaccg cccaacgacc 660
cccgcccatt gacgtcaata atgacgtatg ttcccatagt aacgccaata gggactttcc 720
attgacgtca atgggtggag tatttacggt aaactgccca cttggcagta catcaagtgt 780
atcatatgcc aagtacgccc cctattgacg tcaatgacgg taaatggccc gcctggcatt 840
atgcccagta catgacctta tgggactttc ctacttggca gtacatctac gtattagtca 900
tcgctattac catggtgatg cggttttggc agtacatcaa tgggcgtgga tagcggtttg 960
actcacgggg atttccaagt ctccacccca ttgacgtcaa tgggagtttg ttttggcacc 1020
aaaatcaacg ggactttcca aaatgtcgta acaactccgc cccattgacg caaatgggcg 1080
gtaggcgtgt acggtgggag gtctatataa gcagagctcg tttagtgaac cgtcagatcg 1140
cctggagacg ccatccacgc tgttttgacc tccatagaag acaccgggac cgatccagcc 1200
tccgcggccg ggaacggtgc attggaacgc ggattccccg tgccaagagt gagatctgcc 1260
accatggcgc ccatcacggc ctactcccaa cagacgcggg gcctacttgg ttgcatcatc 1320
actagcctta caggccggga caagaaccag gtcgagggag aggttcaggt ggtttccacc 1380
gcaacacaat ccttcctggc gacctgcgtc aacggcgtgt gttggaccgt ttaccatggt 1440
gctggctcaa agacccttagc cggcccaaag gggccaatca cccagatgta cactaatgtg 1500
gaccaggacc tcgtcggctg gcaggcgccc cccggggcgc gttccttgac accatgcacc 1560
tgtggcagct cagaccttta cttggtcacg agacatgctg acgtcattcc ggtgcgccgg 1620
cggggcgaca gtagggggag cctgctctcc cccaggcctg tctcctactt gaagggctct 1680
tcgggtggtc cactgctctg cccttcgggg cacgctgtgg gcatcttccg ggctgccgta 1740
tgcacccggg gggttgcgaa ggcggtggac tttgtgcccg tagagtccat ggaaactact 1800
atgcggtctc cggtcttcac ggacaactca tcccccccgg ccgtaccgca gtcatttcaa 1860
gtggcccacc tacacgctcc cactggcagc ggcaagagta ctaaagtgcc ggctgcatat 1920
gcagcccaag ggtacaaggt gctcgtcctc aatccgtccg ttgccgctac cttagggttt 1980
ggggcgtata tgtctaaggc acacggtatt gaccccaaca tcagaactgg ggtaaggacc 2040
attaccacag gcgcccccgt cacatactct acctatggca agtttcttgc cgatggtggt 2100
tgctctgggg gcgcttatga catcataata tgtgatgagt gccattcaac tgactcgact 2160

acaatcttgg gcatcggcac agtcctggac caagcggaga cggctggagc gcggcttgtc 2220
gtgctcgcca ccgctacgcc tccgggatcg gtcaccgtgc cacacccaaa catcgaggag 2280
gtggccctgt ctaatactgg agagatcccc ttctatggca aagccatccc cattgaagcc 2340
atcagggggg gaaggcatct cattttctgt cattccaaga agaagtgcga cgagctcgcc 2400
gcaaagctgt caggcctcgg aatcaacgct gtggcgtatt accgggggct cgatgtgtcc 2460
gtcataccaa ctatcggaga cgtcgttgtc gtggcaacag acgctctgat gacgggctat 2520
acgggcgact ttgactcagt gatcgactgt aacacatgtg tcacccagac agtcgacttc 2580
agcttggatc ccaccttcac cattgagacg acgaccgtgc ctcaagacgc agtgtcgcgc 2640
tcgcagcggc ggggtaggac tggcaggggt aggagaggca tctacaggtt tgtgactccg 2700
ggagaacggc cctcgggcat gttcgattcc tcggtcctgt gtgagtgcta tgacgcgggc 2760
tgtgcttggt acgagctcac ccccgccgag acctcggtta ggttgcgggc ctacctgaac 2820
acaccagggt tgcccgtttg ccaggaccac ctggagttct gggagagtgt cttcacaggc 2880
ctcacccaca tagatgcaca cttcttgtcc cagaccaagc aggcaggaga caacttcccc 2940
tacctggtag cataccaagc cacggtgtgc gccagggctc aggcccccac tccatcatgg 3000
gatcaaatgt ggaagtgtct catacggctg aaacctacgc tgcacgggcc aacacccttg 3060
ctgtacaggc tgggagccgt ccaaaatgag gtcaccctca cccaccccat aaccaaatac 3120
atcatggcat gcatgtcggc tgacctggag gtcgtcacta gcacctgggt gctggtgggc 3180
ggagtccttg cagctctggc cgcgtattgc ctgacaacag gcagtgtggt cattgtgggt 3240
aggattatct tgtccgggag gccggctatt gttcccgaca gggagtttct ctaccaggag 3300
ttcgatgaaa tggaagagtg cgcctcgcac ctcccttaca tcgagcaggg aatgcagctc 3360
gccgagcaat tcaagcagaa agcgctcggg ttactgcaaa cagccaccaa acaagcggag 3420
gctgctgctc ccgtggtgga gtccaagtgg cgagcccttg agacattctg ggcgaagcac 3480
atgtggaatt tcatcagcgg gatacagtac ttagcaggct tatccactct gcctgggaac 3540
cccgcaatag catcattgat ggcattcaca gcctctatca ccagcccgct caccacccaa 3600
agtaccctcc tgtttaacat cttggggggg tgggtggctg cccaactcgc ccccccagc 3660
gccgcttcgg ctttcgtggg cgccggcatc gccggtgcgg ctgttggcag cataggcctt 3720
gggaaggtgc ttgtggacat tctggcgggt tatggagcag gagtggccgg cgcgctcgtg 3780
gccttcaagg tcatgagcgg cgagatgccc tccaccgagg acctggtcaa tctacttcct 3840
gccatcctct ctcctggcgc cctggtcgtc ggggtcgtgt gtgcagcaat actgcgtcga 3900
cacgtgggtc cgggagaggg ggctgtgcag tggatgaacc ggctgatagc gttcgcctcg 3960
cggggtaatc atgtttcccc cacgcactat gtgcctgaga gcgacgccgc agcgcgtgtt 4020
actcagatcc tctccagcct taccatcact cagctgctga aaaggctcca ccagtggatt 4080
aatgaagact gctccacacc gtgttccggc tcgtggctaa gggatgtttg ggactggata 4140
tgcacggtgt tgactgactt caagacctgg ctccagtcca agctcctgcc gcagctaccg 4200
ggagtccctt ttttctcgtg ccaacgcggg tacaagggag tctggcgggg agacggcatc 4260
atgcaaacca cctgcccatg tggagcacag atcaccggac atgtcaaaaa cggttccatg 4320
aggatcgtcg ggcctaagac ctgcagcaac acgtggcatg gaacattccc catcaacgca 4380
tacaccacgg gcccctgcac accctctcca gcgccaaact attctagggc gctgtggcgg 4440
gtggccgctg aggagtacgt ggaggtcacg cgggtggggg atttccacta cgtgacgggc 4500
atgaccactg acaacgtaaa gtgcccatgc caggttccgg ctcctgaatt cttcacggag 4560
gtggacggag tgcggttgca caggtacgct ccggcgtgca ggcctctcct acgggaggag 4620
gttacattcc aggtcgggct caaccaatac ctggttgggt cacagctacc atgcgagccc 4680
gaaccggatg tagcagtgct cacttccatg ctcaccgacc cctcccacat cacagcagaa 4740
acggctaagc gtaggttggc caggggggtct ccccccctcct tggccagctc ttcagctagc 4800
cagttgtctg cgccttcctt gaaggcgaca tgcactaccc accatgtctc tccggacgct 4860
gacctcatcg aggccaacct cctgtggcgg caggagatgg gcgggaacat cacccgcgtg 4920
gagtcggaga acaaggtggt agtcctggac tctttcgacc cgcttcgagc ggaggaggat 4980
gagagggaag tatccgttcc ggcggagatc ctgcggaaat ccaagaagtt ccccgcagcg 5040
atgcccatct gggcgcgccc ggattacaac cctccactgt tagagtcctg gaaggacccg 5100
gactacgtcc ctccggtggt gcacgggtgc ccgttgccac ctatcaaggc ccctccaata 5160
ccacctccac ggagaaagag gacggttgtc ctaacagagt cctccgtgtc ttctgcctta 5220
gcggagctcg ctactaagac cttcggcagc tccgaatcat cggccgtcga cagcggcacg 5280
gcgaccgccc ttcctgacca ggcctccgac gacggtgaca aaggatccga cgttgagtcg 5340
tactcctcca tgcccccccct tgagggggaa ccgggggacc ccgatctcag tgacgggtct 5400
tggtctaccg tgagcgagga agctagtgag gatgtcgtct gctgctcaat gtcctacaca 5460

tggacaggcg ccttgatcac gccatgcgct gcggaggaaa gcaagctgcc catcaacgcg 5520
ttgagcaact ctttgctgcg ccaccataac atggtttatg ccacaacatc tcgcagcgca 5580
ggcctgcggc agaagaaggt cacctttgac agactgcaag tcctggacga ccactaccgg 5640
gacgtgctca aggagatgaa ggcgaaggcg tccacagtta aggctaaact cctatccgta 5700
gaggaagcct gcaagctgac gcccccacat tcggccaaat ccaagtttgg ctatggggca 5760
aaggacgtcc ggaacctatc cagcaaggcc gttaaccaca tccactccgt gtggaaggac 5820
ttgctggaag acactgtgac accaattgac accaccatca tggcaaaaaa tgaggttttc 5880
tgtgtccaac cagagaaagg aggccgtaag ccagcccgcc ttatcgtatt cccagatctg 5940
ggagtccgtg tatgcgagaa gatggccctc tatgatgtgg tctccaccct tcctcaggtc 6000
gtgatgggct cctcatacgg attccagtac tctcctgggc agcgagtcga gttcctggtg 6060
aatacctgga aatcaaagaa aaaccccatg ggcttttcat atgacactcg ctgtttcgac 6120
tcaacggtca ccgagaacga catccgtgtt gaggagtcaa tttaccaatg ttgtgacttg 6180
gcccccgaag ccagacaggc cataaaatcg ctcacagagc ggctttatat cggggggtcct 6240
ctgactaatt caaaagggca gaactgcggt tatcgccggt gccgcgcgag cggcgtgctg 6300
acgactagct gcggtaacac cctcacatgt tacttgaagg cctctgcagc ctgtcgagct 6360
gcgaagctcc aggactgcac gatgctcgtg aacgccgccg gccttgtcgt tatctgtgaa 6420
agcgcgggaa cccaagagga cgcggcgagc ctacgagtct tcacggaggc tatgactagg 6480
tactctgccc cccccgggga cccgccccaa ccagaatacg acttggagct gataacatca 6540
tgttcctcca atgtgtcggt cgcccacgat gcatcaggca aaagggtgta ctacctcacc 6600
cgtgatccca ccacccccct cgcacgggct gcgtgggaaa cagctagaca cactccagtt 6660
aactcctggc taggcaacat tatcatgtat gcgcccactt tgtgggcaag gatgattctg 6720
atgactcact tcttctccat ccttctagca caggagcaac ttgaaaaagc cctggactgc 6780
cagatctacg gggcctgtta ctccattgag ccacttgacc tacctcagat cattgaacga 6840
ctccatggcc ttagcgcatt ttcactccat agttactctc caggtgagat caatagggtg 6900
gcttcatgcc tcaggaaact tggggtacca cccttgcgag tctggagaca tcgggccagg 6960
agcgtccgcg ctaggctact gtcccagggg gggagggccg ccacttgtgg caagtacctc 7020
ttcaactggg cagtgaagac caaactcaaa ctcactccaa tcccggctgc gtcccagctg 7080
gacttgtccg gctggttcgt tgctggttac agcgggggag acatatatca cagcctgtct 7140
cgtgcccgac cccgctggtt catgctgtgc ctactcctac tttctgtagg ggtaggcatc 7200
tacctgctcc ccaaccggta aatctagagc tgtgccttct agttgccagc catctgttgt 7260
ttgcccctcc cccgtgcctt ccttgaccct ggaaggtgcc actcccactg tcctttccta 7320
ataaaatgag gaaattgcat cgcattgtct gagtaggtgt cattctattc tggggggtgg 7380
ggtggggcag gacagcaagg gggaggattg ggaagacaat agcaggcatg ctggggatgc 7440
ggtgggctct atggccgatc ggcgcgccgt actgaaatgt gtgggcgtgg cttaagggtg 7500
ggaaagaata tataaggtgg gggtcttatg tagttttgta tctgttttgc agcagccgcc 7560
gccgccatga gcaccaactc gtttgatgga agcattgtga gctcatattt gacaacgcgc 7620
atgcccccat gggccggggt gcgtcagaat gtgatgggct ccagcattga tggtcgcccc 7680
gtcctgcccg caaactctac taccttgacc tacgagaccg tgtctggaac gccgttggag 7740
actgcagcct ccgccgccgc ttcagccgct gcagccaccg cccgcgggat tgtgactgac 7800
tttgctttcc tgagcccgct tgcaagcagt gcagcttccc gttcatccgc ccgcgatgac 7860
aagttgacgg ctcttttggc acaattggat tctttgaccc gggaacttaa tgtcgtttct 7920
cagcagctgt tggatctgcg ccagcaggtt tctgccctga aggcttcctc ccctcccaat 7980
gcggtttaaa acataaataa aaaaccagac tctgtttgga tttggatcaa gcaagtgtct 8040
tgctgtcttt atttaggggt tttgcgcgcg cggtaggccc gggaccagcg gtctcggtcg 8100
ttgagggtcc tgtgtatttt ttccaggacg tggtaaaggt gactctggat gttcagatac 8160
atgggcataa gcccgtctct ggggtggagg tagcaccact gcagagcttc atgctgcggg 8220
gtggtgttgt agatgatcca gtcgtagcag gagcgctggg cgtggtgcct aaaaatgtct 8280
ttcagtagca agctgattgc caggggcagg cccttggtgt aagtgtttac aaagcggtta 8340
agctgggatg ggtgcatacg tggggatatg agatgcatct tggactgtat ttttaggttg 8400
gctatgttcc cagccatatc cctccgggga ttcatgttgt gcagaaccac cagcacagtg 8460
tatccggtgc acttgggaaa tttgtcatgt agcttagaag gaaatgcgtg gaagaacttg 8520
gagacgccct tgtgacctcc aagattttcc atgcattcgt ccataatgat ggcaatgggc 8580
ccacgggcgg cggcctgggc gaagatattt ctgggatcac taacgtcata gttgtgttcc 8640
aggatgagat cgtcataggc catttttaca aagcgcgggc ggagggtgcc agactgcggt 8700
ataatggttc catccggccc aggggcgtag ttaccctcac agatttgcat ttcccacgct 8760

ttgagttcag atggggggat catgtctacc tgcggggcga tgaagaaaac ggtttccggg 8820
gtaggggaga tcagctggga agaaagcagg ttcctgagca gctgcgactt accgcagccg 8880
gtgggcccgt aaatcacacc tattaccggc tgcaactggt agttaagaga gctgcagctg 8940
ccgtcatccc tgagcagggg ggccacttcg ttaagcatgt ccctgactcg catgttttcc 9000
ctgaccaaat ccgccagaag gcgctcgccg cccagcgata gcagttcttg caaggaagca 9060
aagtttttca acggtttgag accgtccgcc gtaggcatgc ttttgagcgt ttgaccaagc 9120
agttccaggc ggtcccacag ctcggtcacc tgctctacgg catctcgatc cagcatatct 9180
cctcgtttcg cgggttgggg cggctttcgc tgtacggcag tagtcggtgc tcgtccagac 9240
gggccagggt catgtctttc cacgggcgca gggtcctcgt cagcgtagtc tgggtcacgg 9300
tgaaggggtg cgctccgggc tgcgcgctgg ccagggtgcg cttgaggctg gtcctgctgg 9360
tgctgaagcg ctgccggtct tcgccctgcg cgtcggccag gtagcatttg accatggtgt 9420
catagtccag cccctccgcg gcgtggccct tggcgcgcag cttgcccttg gaggaggcgc 9480
cgcacgaggg gcagtgcaga cttttgaggg cgtagagctt gggcgcgaga aataccgatt 9540
ccggggagta ggcatccgcg ccgcaggccc cgcagacggt ctcgcattcc acgagccagg 9600
tgagctctgg ccgttcgggg tcaaaaacca ggtttccccc atgctttttg atgcgtttct 9660
tacctctggt ttccatgagc cggtgtccac gctcggtgac gaaaaggctg tccgtgtccc 9720
cgtatacaga cttgagaggc ctgtcctcga gcggtgttcc gcggtcctcc tcgtatagaa 9780
actcggacca ctctgagacg aaggctcgcg tccaggccag cacgaaggag gctaagtggg 9840
aggggtagcg gtcgttgtcc actaggggt ccactcgctc cagggtgtga agacacatgt 9900
cgccctcttc ggcatcaagg aaggtgattg gtttataggt gtaggccacg tgaccgggtg 9960
ttcctgaagg ggggctataa aagggggtgg gggcgcgttc gtcctcactc tcttccgcat 10020
cgctgtctgc gagggccagc tgttggggtg agtactccct ctcaaaagcg ggcatgactt 10080
ctgcgctaag attgtcagtt tccaaaaacg aggaggattt gatattcacc tggcccgcgg 10140
tgatgccttt gagggtggcc gcgtccatct ggtcagaaaa gacaatcttt ttgttgtcaa 10200
gcttggtggc aaacgacccg tagagggcgt tggacagcaa cttggcgatg gagcgcaggg 10260
tttggttttt gtcgcgatcg gcgcgctcct tggccgcgat gtttagctgc acgtattcgc 10320
gcgcaacgca ccgccattcg ggaaagacgg tggtgcgctc gtcgggcact aggtgcacgc 10380
gccaaccgcg gttgtgcagg gtgacaaggt caacgctggt ggctacctct ccgcgtaggc 10440
gctcgttggt ccagcagagg cggccgccct tgcgcgagca gaatggcggt agtgggtcta 10500
gctgcgtctc gtccgggggg tctgcgtcca cggtaaagac cccgggcagc aggcgcgcgt 10560
cgaagtagtc tatcttgcat ccttgcaagt ctagcgcctg ctgccatgcg cgggcggcaa 10620
gcgcgcgctc gtatgggttg agtgggggac cccatggcat ggggtgggtg agcgcggagg 10680
cgtacatgcc gcaaatgtcg taaacgtaga ggggctctct gagtattcca agatatgtag 10740
ggtagcatct tccaccgcgg atgctggcgc gcacgtaatc gtatagttcg tgcgagggag 10800
cgaggaggtc gggaccgagg ttgctacggg cgggctgctc tgctcggaag actatctgcc 10860
tgaagatggc atgtgagttg gatgatatgg ttggacgctg gaagacgttg aagctggcgt 10920
ctgtgagacc taccgcgtca cgcacgaagg aggcgtagga gtcgcgcagc ttgttgacca 10980
gctcggcggt gacctgcacg tctagggcgc agtagtccag ggtttccttg atgatgtcat 11040
acttatcctg tccctttttt ttccacagct cgcggttgag gacaaactct tcgcggtctt 11100
tccagtactc ttggatcgga aacccgtcgg cctccgaacg gtaagagcct agcatgtaga 11160
actggttgac ggcctggtag gcgcagcatc ccttttctac gggtagcgcg tatgcctgcg 11220
cggccttccg gagcgaggtg tgggtgagcg caaaggtgtc cctaaccatg actttgaggt 11280
actggtattt gaagtcagtg tcgtcgcatc cgccctgctc ccagagcaaa aagtccgtgc 11340
gctttttgga acgcgggttt ggcagggcga aggtgacatc gttgaagagt atctttcccg 11400
cgcgaggcat aaagttgcgt gtgatgcgga agggtcccgg cacctcggaa cggttgttaa 11460
ttacctgggc ggcgagcacg atctcgtcaa agccgttgat gttgtggccc acaatgtaaa 11520
gttccaagaa gcgcgggatg cccttgatgg aaggcaattt tttaagttcc tcgtaggtga 11580
gctcttcagg ggagctgagc ccgtgctctg aaagggccca gtctgcaaga tgagggttgg 11640
aagcgacgaa tgagctccac aggtcacggg ccattagcat ttgcaggtgg tcgcgaaagg 11700
tcctaaactg gcgacctatg gccatttttt ctggggtgat gcagtagaag gtaagcgggt 11760
cttgttccca gcggtcccat ccaaggtccg cggctaggtc tcgcgcggcg gtcactagag 11820
gctcatctcc gccgaacttc atgaccagca tgaagggcac gagctgcttc ccaaaggccc 11880
ccatccaagt ataggtctct acatcgtagg tgacaaagag acgctcggtg cgaggatgcg 11940
agccgatcgg gaagaactgg atctcccgcc accagttgga ggagtggctg ttgatgtggt 12000
gaaagtagaa gtccctgcga cgggccgaac actcgtgctg gcttttgtaa aaacgtgcgc 12060

agtactggca gcggtgcacg ggctgtacat cctgcacgag gttgacctga cgaccgcgca 12120
caaggaagca gagtgggaat ttgagcccct cgcctggcgg gtttggctgg tggtcttcta 12180
cttcggctgc ttgtccttga ccgtctggct gctcgagggg agttacggtg gatcggacca 12240
ccacgccgcg cgagcccaaa gtccagatgt ccgcgcgcgg cggtcggagc ttgatgacaa 12300
catcgcgcag atgggagctg tccatggtct ggagctcccg cggcgtcagg tcaggcggga 12360
gctcctgcag gtttacctcg catagccggg tcagggcgcg ggctaggtcc aggtgatacc 12420
tgatttccag gggctggttg gtggcggcgt cgatggcttg caagaggccg catccccgcg 12480
gcgcgactac ggtaccgcgc ggcgggcggt gggccgcggg ggtgtccttg gatgatgcat 12540
ctaaaagcgg tgacgcgggc gggcccccgg aggtaggggg ggctcgggac ccgccgggag 12600
agggggcagg ggcacgtcgg cgccgcgcgc gggcaggagc tggtgctgcg cgcggaggtt 12660
gctggcgaac gcgacgacgc ggcggttgat ctcctgaatc tggcgcctct gcgtgaagac 12720
gacgggcccg gtgagcttga acctgaaaga gagttcgaca gaatcaattt cggtgtcgtt 12780
gacggcggcc tggcgcaaaa tctcctgcac gtctcctgag ttgtcttgat aggcgatctc 12840
ggccatgaac tgctcgatct cttcctcctg gagatctccg cgtccggctc gctccacggt 12900
ggcggcgagg tcgttggaga tgcgggccat gagctgcgag aaggcgttga ggcctccctc 12960
gttccagacg cggctgtaga ccacgccccc ttcggcatcg cgggcgcgca tgaccacctg 13020
cgcgagattg agctccacgt gccgggcgaa gacggcgtag tttcgcaggc gctgaaagag 13080
gtagttgagg gtggtggcgg tgtgttctgc cacgaagaag tacataaccc agcgccgcaa 13140
cgtggattcg ttgatatccc ccaaggcctc aaggcgctcc atggcctcgt agaagtccac 13200
ggcgaagttg aaaaactggg agttgcgcgc cgacacggtt aactcctcct ccagaagacg 13260
gatgagctcg gcgacagtgt cgcgcacctc gcgctcaaag gctacagggg cctcttcttc 13320
ttcttcaatc tcctcttcca taagggcctc cccttcttct tcttctggcg gcggtggggg 13380
aggggggaca cggcggcgac gacggcgcac cgggaggcgg tcgacaaagc gctcgatcat 13440
ctccccgcgg cgacggcgca tggtctcggt gacggcgcgg ccgttctcgc gggggcgcag 13500
ttggaagacg ccgcccgtca tgtcccggtt atgggttggc ggggggctgc cgtgcggcag 13560
ggatacggcg ctaacgatgc atctcaacaa ttgttgtgta ggtactccgc caccgaggga 13620
cctgagcgag tccgcatcga ccggatcgga aaacctctcg agaaaggcgt ctaaccagtc 13680
acagtcgcaa ggtaggctga gcaccgtggc gggcggcagc gggcggcggt cggggttgtt 13740
tctggcggag gtgctgctga tgatgtaatt aaagtaggcg gtcttgagac ggcggatggt 13800
cgacagaagc accatgtcct tgggtccggc ctgctgaatg cgcaggcggt cggccatgcc 13860
ccaggcttcg ttttgacatc ggcgcaggtc tttgtagtag tcttgcatga gcctttctac 13920
cggcacttct tcttctcctt cctcttgtcc tgcatctctt gcatctatcg ctgcggcggc 13980
ggcggagttt ggccgtaggt ggcgccctct tcctcccatg cgtgtgaccc cgaagcccct 14040
catcggctga agcagggcca ggtcggcgac aacgcgctcg gctaatatgg cctgctgcac 14100
ctgcgtgagg gtagactgga agtcgtccat gtccacaaag cggtggtatg cgcccgtgtt 14160
gatggtgtaa gtgcagttgg ccataacgga ccagttaacg gtctggtgac ccggctgcga 14220
gagctcggtg tacctgagac gcgagtaagc ccttgagtca aagacgtagt cgttgcaagt 14280
ccgcaccagg tactggtatc ccaccaaaaa gtgcggcggc ggctggcggt agaggggcca 14340
gcgtagggtg gccggggctc cgggggcgag gtcttccaac ataaggcgat gatatccgta 14400
gatgtacctg gacatccagg tgatgccggc ggcggtggtg gaggcgcgcg gaaagtcacg 14460
gacgcggttc cagatgttgc gcagcggcaa aaagtgctcc atggtcggga cgctctggcc 14520
ggtcaggcgc gcgcagtcgt tgacgctcta gaccgtgcaa aaggagagcc tgtaagcggg 14580
cactcttccg tggtctggtg gataaattcg caagggtatc atggcggacg accggggttc 14640
gaaccccgga tccggccgtc cgccgtgatc catgcggtta ccgcccgcgt gtcgaaccca 14700
ggtgtgcgac gtcagacaac gggggagcgc tccttttggc ttccttccag gcgcggcgga 14760
tgctgcgcta gcttttttgg ccactggccg cgcgcggcgt aagcggttag gctggaaagc 14820
gaaagcatta agtggctcgc tccctgtagc cggagggtta ttttccaagg gttgagtcgc 14880
gggacccccg gttcgagtct cgggccggcc ggactgcggc gaacgggggt ttgcctcccc 14940
gtcatgcaag accccgcttg caaattcctc cggaaacagg gacgagcccc ttttttgctt 15000
ttcccagatg catccggtgc tgcggcagat gcgccccct cctcagcagc ggcaagagca 15060
agagcagcgg cagacatgca gggcaccctc cccttctcct accgcgtcag gaggggcaac 15120
atccgcggct gacgcggcgg cagatggtga ttacgaaccc ccgcggcgcc ggacccggca 15180
ctacttggac ttggaggagg gcgagggcct ggcgcggcta ggagcgccct ctcctgagcg 15240
acacccaagg gtgcagctga agcgtgacac gcgcgaggcg tacgtgccgc ggcagaacct 15300
gtttcgcgac cgcgagggag aggagcccga ggagatgcgg gatcgaaagt tccatgcagg 15360

gcgcgagttg cggcatggcc tgaaccgcga gcggttgctg cgcgaggagg actttgagcc 15420
cgacgcgcgg accgggatta gtcccgcgcg cgcacacgtg gcggccgccg acctggtaac 15480
cgcgtacgag cagacggtga accaggagat taactttcaa aaaagcttta acaaccacgt 15540
gcgcacgctt gtggcgcgcg aggaggtggc tataggactg atgcatctgt gggactttgt 15600
aagcgcgctg gagcaaaacc caaatagcaa gccgctcatg gcgcagctgt tccttatagt 15660
gcagcacagc agggacaacg aggcattcag ggatgcgctg ctaaacatag tagagcccga 15720
gggccgctgg ctgctcgatt tgataaacat tctgcagagc atagtggtgc aggagcgcag 15780
cttgagcctg gctgacaagg tggccgccat taactattcc atgctcagtc tgggcaagtt 15840
ttacgcccgc aagatatacc ataccccttа cgttcccata gacaaggagg taaagatcga 15900
ggggttctac atgcgcatgg cgctgaaggt gcttaccttg agcgacgacc tgggcgttta 15960
tcgcaacgag cgcatccaca aggccgtgag cgtgagccgg cggcgcgagc tcagcgaccg 16020
cgagctgatg cacagcctgc aaagggccct ggctggcacg ggcagcggcg atagagaggc 16080
cgagtcctac tttgacgcgg gcgctgacct gcgctgggcc ccaagccgac gcgccctgga 16140
ggcagctggg gccggacctg ggctggcggt ggcacccgcg cgcgctggca acgtcggcgg 16200
cgtggaggaa tatgacgagg acgatgagta cgagccagag gacggcgagt actaagcggt 16260
gatgtttctg atcagatgat gcaagacgca acggacccgg cggtgcgggc ggcgctgcag 16320
agccagccgt ccggccttaa ctccacggac gactggcgcc aggtcatgga ccgcatcatg 16380
tcgctgactg cgcgcaaccc tgacgcgttc cggcagcagc cgcaggccaa ccggctctcc 16440
gcaattctgg aagcggtggt cccggcgcgc gcaaacccca cgcacgagaa ggtgctggcg 16500
atcgtaaacg cgctggccga aaacagggcc atccggcccg atgaggccgg cctggtctac 16560
gacgcgctgc ttcagcgcgt ggctcgttac aacagcagca acgtgcagac caacctggac 16620
cggctggtgg gggatgtgcg cgaggccgtg gcgcagcgtg agcgcgcgca gcagcagggc 16680
aacctgggct ccatggttgc actaaacgcc ttcctgagta cacagcccgc caacgtgccg 16740
cggggacagg aggactacac caactttgtg agcgcactgc ggctaatggt gactgagaca 16800
ccgcaaagtg aggtgtatca gtccgggcca gactattttt tccagaccag tagacaaggc 16860
ctgcagaccg taaacctgag ccaggctttc aagaacttgc aggggctgtg gggggtgcgg 16920
gctcccacag gcgaccgcgc gaccgtgtct agcttgctga cgcccaactc gcgcctgttg 16980
ctgctgctaa tagcgcccctt cacggacagt ggcagcgtgt cccgggacac atacctaggt 17040
cacttgctga cactgtaccg cgaggccata ggtcaggcgc atgtggacga gcatactttc 17100
caggagatta caagtgttag ccgcgcgctg gggcaggagg acacgggcag cctggaggca 17160
accctgaact acctgctgac caaccggcgg caaaaaatcc cctcgttgca cagtttaaac 17220
agcgaggagg agcgcatttt gcgctatgtg cagcagagcg tgagccttaa cctgatgcgc 17280
gacggggtaa cgcccagcgt ggcgctggac atgaccgcgc gcaacatgga accgggcatg 17340
tatgcctcaa accggccgtt tatcaatcgc ctaatggact acttgcatcg cgcggccgcc 17400
gtgaaccccg agtatttcac caatgccatc ttgaacccgc actggctacc gccccctggt 17460
ttctacaccg gggattcga ggtgcccgag ggtaacgatg gattcctctg ggacgacata 17520
gacgacagcg tgttttcccc gcaaccgcag accctgctag agttgcaaca acgcgagcag 17580
gcagaggcgg cgctgcgaaa ggaaagcttc cgcaggccaa gcagcttgtc cgatctaggc 17640
gctgcggccc cgcggtcaga tgctagtagc ccatttccaa gcttgatagg gtctcttacc 17700
agcactcgca ccacccgccc gcgcctgctg ggcgaggagg agtacctaaa caactcgctg 17760
ctgcagccgc agcgcgaaaa gaacctgcct ccggcgtttc ccaacaacgg gatagagagc 17820
ctagtggaca agatgagtag atggaagacg tatgcgcagg agcacaggga tgtgcccggc 17880
ccgcgcccgc ccacccgtcg tcaaaggcac gaccgtcagc ggggtctggt gtgggaggac 17940
gatgactcgg cagacgacag cagcgtcttg gatttgggag ggagtggcaa cccgtttgca 18000
caccttcgcc ccaggctggg gagaatgttt taaaaaaaag catgatgcaa aataaaaaac 18060
tcaccaaggc catggcaccg agcgttggtt ttcttgtatt ccccttagta tgcggcgcgc 18120
ggcgatgtat gaggaaggtc ctcctccctc ctacgagagc gtggtgagcg cggcgccagt 18180
ggcggcggcg ctgggttcac ccttcgatgc tcccctggac ccgccgttcg tgcctccgcg 18240
gtacctgcgg cctaccgggg ggagaaacag catccgttac tctgagttgg cacccctatt 18300
cgacaccacc cgtgtgtacc ttgtggacaa caagtcaacg gatgtggcat ccctgaacta 18360
ccagaacgac cacagcaact ttctaaccac ggtcattcaa aacaatgact acagcccggg 18420
ggaggcaagc acacagacca tcaatcttga cgaccggtcg cactggggcg gcgacctgaa 18480
aaccatcctg cataccaaca tgccaaatgt gaacgagttc atgtttacca ataagtttaa 18540
ggcgcgggtg atggtgtcgc gctcgcttac taaggacaaa caggtggagc tgaaatacga 18600
gtgggtggag ttcacgctgc ccgagggcaa ctactccgag accatgacca tagaccttat 18660

gaacaacgcg atcgtggagc actacttgaa agtgggcagg cagaacgggg ttctggaaag 18720
cgacatcggg gtaaagtttg acacccgcaa cttcagactg gggtttgacc cagtcactgg 18780
tcttgtcatg cctggggtat atacaaacga agccttccat ccagacatca ttttgctgcc 18840
aggatgcggg gtggacttca cccacagccg cctgagcaac ttgttgggca tccgcaagcg 18900
gcaacccttc caggagggct ttaggatcac ctacgatgac ctggagggtg gtaacattcc 18960
cgcactgttg gatgtggacg cctaccaggc aagcttgaaa gatgacaccg aacagggcgg 19020
gggtggcgca ggcggcggca acaacagtgg cagcggcgcg gaagagaact ccaacgcggc 19080
agctgcggca atgcagccgg tggaggacat gaacgatcat gccattcgcg gcgacacctt 19140
tgccacacgg gcggaggaga agcgcgctga ggccgaggca gcggccgaag ctgccgcccc 19200
cgctgcggag gctgcacaac ccgaggtcga gaagcctcag aagaaaccgg tgattaaacc 19260
cctgacagag gacagcaaga aacgcagtta caacctaata agcaatgaca gcaccttcac 19320
ccagtaccgc agctggtacc ttgcatacaa ctacggcgac cctcaggccg ggatccgctc 19380
atggaccctg ctttgcactc ctgacgtaac ctgcggctcg gagcaggtat actggtcgtt 19440
gcccgacatg atgcaagacc ccgtgacctt ccgctccacg cgccagatca gcaactttcc 19500
ggtggtgggc gccgagctgt tgcccgtgca ctccaagagc ttctacaacg accaggccgt 19560
ctactcccag ctcatccgcc agtttacctc tctgacccac gtgttcaatc gctttcccga 19620
gaaccagatt ttggcgcgcc cgccagcccc caccatcacc accgtcagtg aaaacgttcc 19680
tgctctcaca gatcacggga cgctaccgct gcgcaacagc atcggaggag tccagcgagt 19740
gaccattact gacgccagac gccgcacctg cccctacgtt tacaaggccc tgggcatagt 19800
ctcgccgcgc gtcctatcga gccgcacttt ttgagcaagc atgtccatcc ttatatcgcc 19860
cagcaataac acaggctggg gcctgcgctt cccaagcaag atgtttggcg gggccaagaa 19920
gcgctccgac caacacccag tgcgcgtgcg cgggcactac cgcgcgccct ggggcgcgca 19980
caaacgcggc cgcactgggc gcaccaccgt cgatgacgcc atcgacgcgg tggtggagga 20040
ggcgcgcaac tacacgccca cgccgccgcc agtgtccacc gtggacgcgg ccattcagac 20100
cgtggtgcgc ggagcccggc gctacgctaa aatgaagaga cggcggaggc gcgtagcacg 20160
tcgccaccgc cgccgacccg gcactgccgc ccaacgcgcg gcggcggccc tgcttaaccg 20220
cgcacgtcgc accggccgac gggcggccat gcgagccgct cgaaggctgg ccgcgggtat 20280
tgtcactgtg ccccccaggt ccaggcgacg agcggccgcc gcagcagccg cggccattag 20340
tgctatgact cagggtcgca ggggcaacgt gtactgggtg cgcgactcgg ttagcggcct 20400
gcgcgtgccc gtgcgcaccc gcccccgcg caactagatt gcaataaaaa actacttaga 20460
ctcgtactgt tgtatgtatc cagcggcggc ggcgcgcatc gaagctatgt ccaagcgcaa 20520
aatcaaagaa gagatgctcc aggtcatcgc gccggagatc tatggccccc cgaagaagga 20580
agagcaggat tacaagcccc gaaagctaaa gcgggtcaaa aagaaaaaga aagatgatga 20640
tgatgatgaa cttgacgacg aggtggaact gttgcacgcg accgcgccca ggcgacgggt 20700
acagtggaaa ggtcgacgcg taagacgtgt tttgcgaccc ggcaccaccg tagtctttac 20760
gcccggtgag cgctccaccc gcacctacaa gcgcgtgtat gatgaggtgt acggcgacga 20820
ggacctgctt gagcaggcca acgagcgcct cggggagttt gcctacggaa agcggcataa 20880
ggacatgctg gcgttgccgc tggacgaggg caacccaaca cctagcctaa agcccgtgac 20940
actgcagcag gtgctgcccg cgcttgcacc gtccgaagaa aagcgcggcc taaagcgcga 21000
gtctggtgac ttggcaccca ccgtgcagct gatggtaccc aagcgtcagc gactggaaga 21060
tgtcttggaa aaaatgaccg tggagcctgg gctggagccc gaggtccgcg tgcggccaat 21120
caagcaggtg gcaccgggac tgggcgtgca gaccgtggac gttcagatac ccaccaccag 21180
tagcactagt attgccactg ccacagaggg catggagaca caaacgtccc cggttgcctc 21240
ggcggtggca gatgccgcgg tgcaggcggc cgctgcggcc gcgtccaaga cctctacgga 21300
ggtgcaaacg gacccgtgga tgtttcgtgt ttcagccccc cggcgtccgc gccgttcaag 21360
gaagtacggc gccgccagcg cgctactgcc cgaatatgcc ctacatcctt ccatcgcgcc 21420
tacccccggc tatcgtggct acacctaccg ccccagaaga cgagcaacta cccgacgccg 21480
aaccaccact ggaacccgcc gccgccgtcg ccgtcgccag cccgtgctgg ccccgatttc 21540
cgtgcgcagg gtggctcgcg aaggaggcag gaccctggtg ctgccaacag cgcgctacca 21600
ccccagcatc gtttaaaagc cggtctttgt ggttcttgca gatatggccc tcacctgccg 21660
cctccgtttc ccggtgccgg gattccgagg aagaatgcac cgtaggaggg gcatggccgg 21720
ccacggcctg acgggcggca tgcgtcgtgc gcaccaccgg cggcggcgcg cgtcgcaccg 21780
tcgcatgcgc ggcggtatcc tgcccctcct tattccactg atcgccgcgg cgattggcgc 21840
cgtgcccgga attgcatccg tggccttgca ggcgcagaga cactgattaa aaacaagtta 21900
catgtggaaa aatcaaaata aaagtctgga ctctcacgct cgcttggtcc tgtaactatt 21960

ttgtagaatg gaagacatca actttgcgtc actggccccg cgacacggct cgcgcccgtt 22020
catgggaaac tggcaagata tcggcaccag caatatgagc ggtggcgcct tcagctgggg 22080
ctcgctgtgg agcggcatta aaaatttcgg ttccgccgtt aagaactatg gcagcaaagc 22140
ctggaacagc agcacaggcc agatgctgag ggacaagttg aaagagcaaa atttccaaca 22200
aaaggtggta gatggcctgg cctctggcat tagcggggtg gtggacctgg ccaaccaggc 22260
agtgcaaaat aagattaaca gtaagcttga tccccgccct cccgtagagg agcctccacc 22320
ggccgtggag acagtgtctc cagaggggcg tggcgaaaag cgtccgcgac ccgacaggga 22380
agaaactctg gtgacgcaaa tagacgagcc tccctcgtac gaggaggcac taaagcaagg 22440
cctgcccacc acccgtccca tcgcgcccat ggctaccgga gtgctgggcc agcacacacc 22500
cgtaacgctg gacctgcctc cccccgccga cacccagcag aaacctgtgc tgccaggccc 22560
gtccgccgtt gttgtaaccc gtcctagccg cgcgtccctg cgccgcgccg ccagcggtcc 22620
gcgatcgttg cggcccgtag ccagtggcaa ctggcaaagc acactgaaca gcatcgtggg 22680
tttgggggtg caatccctga agcgccgacg atgcttctga tagctaacgt gtcgtatgtg 22740
tgtcatgtat gcgtccatgt cgccgccaga ggagctgctg agccgccgcg cgcccgcttt 22800
ccaagatggc taccccttcg atgatgccgc agtggtctta catgcacatc tcgggccagg 22860
acgcctcgga gtacctgagc cccgggctgg tgcagttcgc ccgcgccacc gagacgtact 22920
tcagcctgaa taacaagttt agaaacccca cggtggcgcc tacgcacgac gtgaccacag 22980
accggtctca gcgtttgacg ctgcggttca tccccgtgga ccgcgaggat actgcgtact 23040
cgtacaaggc gcggttcacc ctagctgtgg gtgataaccg tgtgctagac atggcttcca 23100
cgtactttga catccgcggc gtgctggaca ggggccctac ttttaagccc tactctggca 23160
ctgcctacaa cgcactggcc cccaagggtg cccccaactc gtgcgagtgg gaacaaaatg 23220
aaactgcaca agtggatgct caagaacttg acgaagagga gaatgaagcc aatgaagctc 23280
aggcgcgaga acaggaacaa gctaagaaaa cccatgtata tgcccaggct ccactgtccg 23340
gaataaaaat aactaaagaa ggtctacaaa taggaactgc cgacgccaca gtagcaggtg 23400
ccggcaaaga aattttcgca gacaaaactt ttcaacctga accacaagta ggagaatctc 23460
aatggaacga agcggatgcc acagcagctg gtggaagggt tcttaaaaag acaactccca 23520
tgaaaccctg ctatggctca tacgctagac ccaccaattc caacggcgga cagggcgtta 23580
tggttgaaca aaatggtaaa ttggaaagtc aagtcgaaat gcaatttttt tccacatcca 23640
caaatgccac aaatgaagtt aacaatatac aaccaacagt tgtattgtac agcgaagatg 23700
taaacatgga aactccagat actcatcttt cttataaacc taaaatgggg gataaaaatg 23760
ccaaagtcat gcttggacaa caagcaatgc caaacagacc aaattacatt gcttttagag 23820
acaattttat tggtctcatg tattacaaca gcacaggtaa catgggtgtc cttgctggtc 23880
aggcatcgca gttgaacgct gttgtagatt tgcaagacag aaacacagag ctgtcctacc 23940
agcttttgct tgattcaatt ggcgacagaa caagatactt ttcaatgtgg aatcaagctg 24000
ttgacagcta tgatccagat gtcagaatta ttgagaacca tggaactgag gatgagttgc 24060
caaattattg ctttcctctt ggtggaattg ggattactga cacttttcaa gctgttaaaa 24120
caactgctgc taacggggac caaggcaata ctacctggca aaaagattca acatttgcag 24180
aacgcaatga aatagggggtg ggaaataact ttgccatgga aattaacctg aatgccaacc 24240
tatggagaaa tttcctttac tccaatattg cgctgtacct gccagacaag ctaaaataca 24300
accccaccaa tgtggaaata tctgacaacc ccaacaccta cgactacatg aacaagcgag 24360
tggtggctcc tgggcttgta gactgctaca ttaaccttgg ggcgcgctgg tctctggact 24420
acatggacaa cgttaatccc tttaaccacc accgcaatgc gggcctgcgt taccgctcca 24480
tgttgttggg aaacggccgc tacgtgccct ttcacattca ggtgccccaa aagttttttg 24540
ccattaaaaa cctcctcctc ctgccaggct catacacata tgaatggaac ttcaggaagg 24600
atgttaacat ggttctgcag agctctctgg gaaacgacct tagagttgac ggggctagca 24660
ttaagtttga cagcatttgt ctttacgcca ccttcttccc catggcccac aacacggcct 24720
ccacgctgga agccatgctc agaaatgaca ccaacgacca gtcctttaat gactaccttt 24780
ccgccgccaa catgctatat cccatacccg ccaacgccac caacgtgccc atctccatcc 24840
catcgcgcaa ctgggcagca tttcgcggtt gggccttcac acgcttgaag acaaaggaaa 24900
ccccttccct gggatcaggc tacgaccctt actacaccta ctctggctcc ataccatacc 24960
ttgacggaac cttctatctt aatcacacct ttaagaaggt ggccattact tttgactctt 25020
ctgttagctg gccgggcaac gaccgcctgc ttactcccaa tgagtttgag attaagcgct 25080
cagttgacgg ggagggctat aacgtagctc agtgcaacat gacaaaggac tggttcctag 25140
tgcagatgtt ggccaactac aatattggct accagggctt ctacattcca gaaagctaca 25200
aagaccgcat gtactcgttc ttcagaaact tccagcccat gagccggcaa gtggtggacg 25260

atactaaata caaagattat cagcaggttg gaattatcca ccagcataac aactcaggct 25320
tcgtaggcta cctcgctccc accatgcgcg agggacaagc ttaccccgct aatgttccct 25380
acccactaat aggcaaaacc gcggttgata gtattaccca gaaaaagttt ctttgcgacc 25440
gcaccctgtg gcgcatcccc ttctccagta actttatgtc catgggtgcg ctcacagacc 25500
tgggccaaaa ccttctctac gcaaactccg cccacgcgct agacatgacc tttgaggtgg 25560
atcccatgga cgagcccacc cttctttatg ttttgtttga agtctttgac gtggtccgtg 25620
tgcaccagcc gcaccgcggc gtcatcgaga ccgtgtacct gcgcacgccc ttctcggccg 25680
gcaacgccac aacataaaga agcaagcaac atcaacaaca gctgccgcca tgggctccag 25740
tgagcaggaa ctgaaagcca ttgtcaaaga tcttggttgt gggccatatt ttttgggcac 25800
ctatgacaag cgcttcccag gctttgtttc cccacacaag ctcgcctgcg ccatagttaa 25860
cacggccggt cgcgagactg gggcgtaca ctggatggcc tttgcctgga acccgcgctc 25920
aaaaacatgc tacctctttg agccctttgg ctttctgac caacgtctca agcaggttta 25980
ccagtttgag tacgagtcac tcctgcgccg tagcgccatt gcctcttccc ccgaccgctg 26040
tataacgctg gaaaagtcca cccaaagcgt gcaggggccc aactcggccg cctgtggcct 26100
attctgctgc atgtttctcc acgcctttgc caactggccc caaactccca tggatcacaa 26160
ccccaccatg aaccttatta ccggggtacc caactccatg cttaacagtc cccaggtaca 26220
gcccaccctg cgccgcaacc aggaacagct ctacagcttc ctggagcgcc actcgcccta 26280
cttccgcagc cacagtgcgc aaattaggag cgccacttct tttgtcact tgaaaaacat 26340
gtaaaaataa tgtactagga gacactttca ataaaggcaa atgtttttat ttgtacactc 26400
tcgggtgatt atttaccccc acccttgccg tctgcgccgt ttaaaaatca aaggggttct 26460
gccgcgcatc gctatgcgcc actggcaggg acacgttgcg atactggtgt ttagtgctcc 26520
acttaaactc aggcacaacc atccgcggca gctcggtgaa gttttcactc cacaggctgc 26580
gcaccatcac caacgcgttt agcaggtcgg gcgccgatat cttgaagtcg cagttggggc 26640
ctccgccctg cgcgcgcgag ttgcgataca cagggttaca gcactggaac actatcagcg 26700
ccgggtggtg cacgctggcc agcacgctct tgtcggagat cagatccgcg tccaggtcct 26760
ccgcgttgct cagggcgaac ggagtcaact ttggtagctg ccttcccaaa aagggtgcat 26820
gcccaggctt tgagttgcac tcgcaccgta gtggcatcag aaggtgaccg tgcccagtct 26880
gggcgttagg atacagcgcc tgcatgaaag ccttgatctg cttaaaagcc acctgagcct 26940
ttgcgccttc agagaagaac atgccgcaag acttgccgga aaactgattg gccggacagg 27000
ccgcgtcatg cacgcagcac cttgcgtcgg tgttggagat ctgcaccaca tttcggcccc 27060
accggttctt cacgatcttg gccttgctag actgctcctt cagcgcgcgc tgcccgtttt 27120
cgctcgtcac atccatttca atcacgtgct ccttatttat cataatgctc ccgtgtagac 27180
acttaagctc gccttcgatc tcagcgcagc ggtgcagcca caacgcgcag cccgtgggct 27240
cgtggtgctt gtaggttacc tctgcaaacg actgcaggta cgcctgcagg aatcgcccca 27300
tcatcgtcac aaaggtcttg ttgctggtga aggtcagctg caacccgcgg tgctcctcgt 27360
ttagccaggt cttgcatacg gccgccagag cttccacttg gtcaggcagt agcttgaagt 27420
ttgcctttag atcgttatcc acgtggtact tgtccatcaa cgcgcgcgca gcctccatgc 27480
ccttctccca cgcagacacg atcggcaggc tcagcgggtt tatcaccgtg ctttcacttt 27540
ccgcttcact ggactcttcc ttttcctctt gcatccgcat accccgcgcc actgggtcgt 27600
cttcattcag ccgccgcacc gtgcgcttac ctcccttgcc gtgcttgatt agcaccggtg 27660
ggttgctgaa acccaccatt tgtagcgcca catcttctct ttcttcctcg ctgtccacga 27720
tcacctctgg ggatggcggg cgctcgggct tgggagaggg gcgcttcttt ttcttttgg 27780
acgcaatggc caaatccgcc gtcgaggtcg atggccgcgg gctgggtgtg cgcggcacca 27840
gcgcatcttg tgacgagtct tcttcgtcct cggactcgag acgccgcctc agccgctttt 27900
ttgggggcgc gcggggaggc ggcggcgacg gcgacgggga cgagacgtcc tccatggttg 27960
gtggacgtcg cgccgcaccg cgtccgcgct cggggtggt ttcgcgctgc tcctcttccc 28020
gactggccat ttccttctcc tataggcaga aaaagatcat ggagtcagtc gagaaggagg 28080
acagcctaac cgccccctt gagttcgcca ccaccgcctc caccgatgcc gccaacgcgc 28140
ctaccacctt ccccgtcgag gcaccccgc ttgaggagga ggaagtgatt atcgagcagg 28200
acccaggttt tgtaagcgaa gacgacgaag atcgctcagt accaacagag gataaaaagc 28260
aagaccagga cgacgcagag gcaaacgagg aacaagtcgg gcggggggac caaaggcatg 28320
gcgactacct agatgtggga gacgacgtgc tgttgaagca tctgcagcgc cagtgcgcca 28380
ttatctgcga cgcgttgcaa gagcgcagcg atgtgcccct cgccatagcg gatgtcagcc 28440
ttgcctacga acgccacctg ttctcaccgc gcgtaccccc caaacgccaa gaaaacggca 28500
catgcgagcc caacccgcgc ctcaacttct accccgtatt tgccgtgcca gaggtgcttg 28560

ccacctatca catctttttc caaaactgca agatacccct atcctgccgt gccaaccgca 28620
gccgagcgga caagcagctg gccttgcggc agggcgctgt catacctgat atcgcctcgc 28680
tcgacgaagt gccaaaaatc tttgagggtc ttggacgcga cgagaagcgc gcggcaaacg 28740
ctctgcaaca agaaaacagc gaaaatgaaa gtcactgtgg agtgctggtg gaacttgagg 28800
gtgacaacgc gcgcctagcc gtgctgaaac gcagcatcga ggtcacccac tttgcctacc 28860
cggcacttaa cctacccccc aaggttatga gcacagtcat gagcgagctg atcgtgcgcc 28920
gtgcacgacc cctggagagg gatgcaaact tgcaagaaca aaccgaggag ggcctacccg 28980
cagttggcga tgagcagctg gcgcgctggc ttgagacgcg cgagcctgcc gacttggagg 29040
agcgacgcaa gctaatgatg gccgcagtgc ttgttaccgt ggagcttgag tgcatgcagc 29100
ggttctttgc tgacccggag atgcagcgca agctagagga aacgttgcac tacacctttc 29160
gccagggcta cgtgcgccag gcctgcaaaa tttccaacgt ggagctctgc aacctggtct 29220
cctaccttgg aattttgcac gaaaaccgcc ttgggcaaaa cgtgcttcat tccacgctca 29280
agggcgaggc gcgccgcgac tacgtccgcg actgcgttta cttatttctg tgctacacct 29340
ggcaaacggc catgggcgtg tggcagcagt gcctggagga gcgcaacctg aaggagctgc 29400
agaagctgct aaagcaaaac ttgaaggacc tatggacggc cttcaacgag cgctccgtgg 29460
ccgcgcacct ggcggacatt atcttccccg aacgcctgct taaaaccctg caacagggtc 29520
tgccagactt caccagtcaa agcatgttgc aaaactttag gaactttatc ctagagcgtt 29580
caggaattct gcccgccacc tgctgtgcgc ttcctagcga ctttgtgccc attaagtacc 29640
gtgaatgccc tccgccgctt tggggtcact gctaccttct gcagctagcc aactaccttg 29700
cctaccactc cgacatcatg gaagacgtga gcggtgacgg cctactggag tgtcactgtc 29760
gctgcaacct atgcaccccg caccgctccc tggtctgcaa ttcacaactg cttagcgaaa 29820
gtcaaattat cggtaccttt gagctgcagg gtccctcgcc tgacgaaaag tccgcggctc 29880
cggggttgaa actcactccg gggctgtgga cgtcggctta ccttcgcaaa tttgtacctg 29940
aggactacca cgcccacgag attaggttct acgaagacca atcccgcccg ccaaatgcgg 30000
agcttaccgc ctgcgtcatt acccagggcc acatccttgg ccaattgcaa gccattaaca 30060
aagcccgcca agagtttctg ctacgaaagg gacggggggt ttacttggac ccccagtccg 30120
gcgaggagct caacccaatc cccccgccgc cgcagcccta tcagcagccg cgggcccttg 30180
cttcccagga tggcacccaa aaagaagctg cagctgccgc cgccgccacc cacggacgag 30240
gaggaatact gggacagtca ggcagaggag gttttggacg aggaggagga gatgatggaa 30300
gactgggaca gcctagacga ggaagcttcc gaggccgaag aggtgtcaga cgaaacaccg 30360
tcaccctcgg tcgcattccc ctcgccggcg ccccagaaat cggcaaccgt tcccagcatt 30420
gctacaacct ccgctcctca ggcgccgccg gcactgcccg ttcgccgacc caaccgtaga 30480
tgggacacca ctggaaccag ggccggtaag tctaagcagc cgccgccgtt agcccaagag 30540
caacaacagc gccaaggcta ccgctcgtgg cgcgtgcaca agaacgccat agttgcttgc 30600
ttgcaagact gtgggggcaa catctccttc gcccgccgct ttcttctcta ccatcacggc 30660
gtggccttcc cccgtaacat cctgcattac taccgtcatc tctacagccc ctactgcacc 30720
ggcggcagcg gcagcaacag cagcggccac gcagaagcaa aggcgaccgg atagcaagac 30780
tctgacaaag cccaagaaat ccacagcggc ggcagcagca ggaggaggag cactgcgtct 30840
ggcgcccaac gaacccgtat cgacccgcga gcttagaaac aggatttttc ccactctgta 30900
tgctatattt caacagagca ggggccaaga acaagagctg aaaataaaaa acaggtctct 30960
gcgctccctc acccgcagct gcctgtatca caaaagcgaa gatcagcttc ggcgcacgct 31020
ggaagacgcg gaggctctct tcagcaaata ctgcgcgctg actcttaagg actagtttcg 31080
cgccctttct caaatttaag cgcgaaaact acgtcatctc cagcggccac acccggcgcc 31140
agcacctgtc gtcagcgcca ttatgagcaa ggaaattccc acgccctaca tgtggagtta 31200
ccagccacaa atgggacttg cggctggagc tgcccaagac tactcaaccc gaataaacta 31260
catgagcgcg ggaccccaca tgatatcccg ggtcaacgga atccgcgccc accgaaaccg 31320
aattctcctc gaacaggcgg ctattaccac cacacctcgt aataacctta atccccgtag 31380
ttggcccgct gccctggtgt accaggaaag tcccgctccc accactgtgg tacttcccag 31440
agacgcccag gccgaagttc agatgactaa ctcaggggcg cagcttgcgg gcggctttcg 31500
tcacagggtg cggtcgcccg ggcagggtat aactcacctg aaaatcagag ggcgaggtat 31560
tcagctcaac gacgagtcgg tgagctcctc tcttggtctc cgtccggacg ggacatttca 31620
gatcggcggc gctggccgct cttcatttac gccccgtcag gcgatcctaa ctctgcagac 31680
ctcgtcctcg gagccgcgct ccggaggcat tggaactcta caatttattg aggagttcgt 31740
gccttcggtt tacttcaacc cctttctgg acctcccggc cactacccgg accagtttat 31800
tcccaacttt gacgcggtaa aagactcggc ggacggctac gactgaatga ccagtggaga 31860

ggcagagcaa ctgcgcctga cacacctcga ccactgccgc cgccacaagt gctttgcccg 31920
cggctccggt gagttttgtt actttgaatt gcccgaagag catatcgagg gcccggcgca 31980
cggcgtccgg ctcaccaccc aggtagagct tacacgtagc ctgattcggg agtttaccaa 32040
gcgcccccctg ctagtggagc gggagcgggg tccctgtgtt ctgaccgtgg tttgcaactg 32100
tcctaaccct ggattacatc aagatcttat tccattcaac taacaataaa cacacaataa 32160
attacttact taaaatcagt cagcaaatct ttgtccagct tattcagcat cacctccttt 32220
ccctcctccc aactctggta tttcagcagc cttttagctg cgaactttct ccaaagtcta 32280
aatgggatgt caaattcctc atgttcttgt ccctccgcac ccactatctt catattgttg 32340
cagatgaaac gcgccagacc gtctgaagac accttcaacc ctgtgtaccc atatgacacg 32400
gaaaccggcc ctccaactgt gcctttcctt acccctccct ttgtgtcgcc aaatgggttc 32460
caagaaagtc cccccggagt gctttctttg cgtctttcag aacctttggt tacctcacac 32520
ggcatgcttg cgctaaaaat gggcagcggc ctgtccctgg atcaggcagg caaccttaca 32580
tcaaatacaa tcactgtttc tcaaccgcta aaaaaaacaa agtccaatat aactttggaa 32640
acatccgcgc cccttacagt cagctcaggc gccctaacca tggccacaac ttcgcctttg 32700
gtggtctctg acaacactct taccatgcaa tcacaagcac cgctaaccgt gcaagactca 32760
aaacttagca ttgctaccaa agagccactt acagtgttag atggaaaact ggccctgcag 32820
acatcagccc ccctctctgc cactgataac aacgccctca ctatcactgc ctcacctcct 32880
cttactactg caaatggtag tctggctgtt accatggaaa acccacttta caacaacaat 32940
ggaaaacttg ggctcaaaat tggcggtcct ttgcaagtgg ccaccgactc acatgcacta 33000
acactaggta ctggtcaggg ggttgcagtt cataacaatt tgctacatac aaaagttaca 33060
ggcgcaatag ggtttgatac atctggcaac atggaactta aaactggaga tggcctctat 33120
gtggatagcg ccggtcctaa ccaaaaacta catattaatc taaataccac aaaaggcctt 33180
gcttttgaca acaccgcaat aacaattaac gctggaaaag ggttggaatt tgaaacagac 33240
tcctcaaacg gaaatcccat aaaaacaaaa attggatcag gcatacaata taataccaat 33300
ggagctatgg ttgcaaaact tggaacaggc ctcagttttg acagctccgg agccataaca 33360
atgggcagca taaacaatga cagacttact ctttggacaa caccagaccc atccccaaat 33420
tgcagaattg cttcagataa agactgcaag ctaactctgg cgctaacaaa atgtggcagt 33480
caaattttgg gcactgtttc agctttggca gtatcaggta atatggcctc catcaatgga 33540
actctaagca gtgtaaactt ggttcttaga tttgatgaca acggagtgct tatgtcaaat 33600
tcatcactgg acaaacagta ttggaacttt agaaacgggg actccactaa cggtcaacca 33660
tacacttatg ctgttgggtt tatgccaaac ctaaaagctt acccaaaaac tcaaagtaaa 33720
actgcaaaaa gtaatattgt tagccaggtg tatcttaatg gtgacaagtc taaaccattg 33780
cattttacta ttacgctaaa tggaacagat gaaaccaacc aagtaagcaa atactcaata 33840
tcattcagtt ggtcctggaa cagtggacaa tacactaatg acaaatttgc caccaattcc 33900
tataccttct cctacattgc ccaggaataa agaatcgtga acctgttgca tgttatgttt 33960
caacgtgttt atttttcaat tgcagaaaat ttcaagtcat ttttcattca gtagtatagc 34020
cccaccacca catagcttat actaatcacc gtaccttaat caaactcaca gaaccctagt 34080
attcaacctg ccacctccct cccaacacac agagtacaca gtcctttctc cccggctggc 34140
cttaaacagc atcatatcat gggtaacaga catattctta ggtgttatat tccacacggt 34200
ctcctgtcga gccaaacgct catcagtgat gttaataaac tccccgggca gctcgcttaa 34260
gttcatgtcg ctgtccagct gctgagccac aggctgctgt ccaacttgcg gttgctcaac 34320
gggcggcgaa ggagaagtcc acgcctacat gggggtagag tcataatcgt gcatcaggat 34380
agggcggtgg tgctgcagca gcgcgcgaat aaactgctgc cgccgccgct ccgtcctgca 34440
ggaatacaac atggcagtgg tctcctcagc gatgattcgc accgcccgca gcataaggcg 34500
ccttgtcctc cgggcacagc agcgcaccct gatctcactt aagtcagcac agtaactgca 34560
gcacagtacc acaatattgt ttaaaatccc acagtgcaag gcgctgtatc caaagctcat 34620
ggcggggacc acagaaccca cgtggccatc ataccacaag cgcaggtaga ttaagtggcg 34680
acccctcata aacacgctgg acataaacat tacctctttt ggcatgttgt aattcaccac 34740
ctcccggtac catataaacc tctgattaaa catggcgcca tccaccacca tcctaaacca 34800
gctggccaaa acctgcccgc cggctatgca ctgcagggaa ccgggactgg aacaatgaca 34860
gtggagagcc caggactcgt aaccatggat catcatgctc gtcatgatat caatgttggc 34920
acaacacagg cacacgtgca tacacttcct caggattaca agctcctccc gcgtcagaac 34980
catatcccag ggaacaaccc attcctgaat cagcgtaaat cccacactgc agggaagacc 35040
tcgcacgtaa ctcacgttgt gcattgtcaa agtgttacat tcgggcagca gcggatgatc 35100
ctccagtatg gtagcgcggg tttctgtctc aaaaggaggt agacgatccc tactgtacgg 35160

agtgcgccga gacaaccgag atcgtgttgg tcgtagtgtc atgccaaatg gaacgccgga 35220
cgtagtcata tttcctgaag caaaaccagg tgcgggcgtg acaaacagat ctgcgtctcc 35280
ggtctcgccg cttagatcgc tctgtgtagt agttgtagta tatccactct ctcaaagcat 35340
ccaggcgccc cctggcttcg ggttctatgt aaactccttc atgcgccgct gccctgataa 35400
catccaccac cgcagaataa gccacaccca gccaacctac acattcgttc tgcgagtcac 35460
acacgggagg agcgggaaga gctggaagaa ccatgttttt tttttattc caaaagatta 35520
tccaaaacct caaaatgaag atctattaag tgaacgcgct cccctccggt ggcgtggtca 35580
aactctacag ccaaagaaca gataatggca tttgtaagat gttgcacaat ggcttccaaa 35640
aggcaaacgg ccctcacgtc caagtggacg taaaggctaa acccttcagg gtgaatctcc 35700
tctataaaca ttccagcacc ttcaaccatg cccaaataat tctcatctcg ccaccttctc 35760
aatatatctc taagcaaatc ccgaatatta agtccggcca ttgtaaaaat ctgctccaga 35820
gcgccctcca ccttcagcct caagcagcga atcatgattg caaaaattca ggttcctcac 35880
agacctgtat aagattcaaa agcggaacat taacaaaaat accgcgatcc cgtaggtccc 35940
ttcgcagggc cagctgaaca taatcgtgca ggtctgcacg gaccagcgcg gccacttccc 36000
cgccaggaac catgacaaaa gaacccacac tgattatgac acgcatactc ggagctatgc 36060
taaccagcgt agccccgatg taagcttgtt gcatgggcgg cgatataaaa tgcaaggtgc 36120
tgctcaaaaa atcaggcaaa gcctcgcgca aaaaagaaag cacatcgtag tcatgctcat 36180
gcagataaag gcaggtaagc tccggaacca ccacagaaaa agacaccatt tttctctcaa 36240
acatgtctgc gggtttctgc ataaacacaa aataaaataa caaaaaaaca tttaaacatt 36300
agaagcctgt cttacaacag gaaaaacaac ccttataagc ataagacgga ctacggccat 36360
gccggcgtga ccgtaaaaaa actggtcacc gtgattaaaa agcaccaccg acagctcctc 36420
ggtcatgtcc ggagtcataa tgtaagactc ggtaaacaca tcaggttgat tcacatcggt 36480
cagtgctaaa aagcgaccga aatagcccgg gggaatacat acccgcaggc gtagagacaa 36540
cattacagcc cccataggag gtataacaaa attaatagga gagaaaaaca cataaacacc 36600
tgaaaaaccc tcctgcctag gcaaaatagc accctcccgc tccagaacaa catacagcgc 36660
ttccacagcg gcagccataa cagtcagcct taccagtaaa aaagaaaacc tattaaaaaa 36720
acaccactcg acacggcacc agctcaatca gtcacagtgt aaaaaagggc caagtgcaga 36780
gcgagtatat ataggactaa aaaatgacgt aacggttaaa gtccacaaaa aacacccaga 36840
aaaccgcacg cgaacctacg cccagaaacg aaagccaaaa aacccacaac ttcctcaaat 36900
cgtcacttcc gtttcccac gttacgtcac ttcccatttt aagaaaacta caattcccaa 36960
cacatacaag ttactccgcc ctaaaaccta cgtcacccgc cccgttccca cgccccgcgc 37020
cacgtcacaa actccacccc ctcattatca tattggcttc aatccaaaat aaggtatatt 37080
attgatgatg 37090

<210> 5
<211> 5955
<212> DNA
<213> Artificial Sequence

<220>
<223> NS cDNA sequence

<221> CDS
<222> (1)...(5955)

<400> 5
atg gcg ccc atc acg gcc tac tcc caa cag acg cgg ggc cta ctt ggt 48
Met Ala Pro Ile Thr Ala Tyr Ser Gln Gln Thr Arg Gly Leu Leu Gly
1 5 10 15

tgc atc atc act agc ctt aca ggc cgg gac aag aac cag gtc gag gga 96
Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
20 25 30

gag gtt cag gtg gtt tcc acc gca aca caa tcc ttc ctg gcg acc tgc 144

```
Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
        35                  40                  45

gtc aac ggc gtg tgt tgg acc gtt tac cat ggt gct ggc tca aag acc      192
Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
    50                  55                  60

tta gcc ggc cca aag ggg cca atc acc cag atg tac act aat gtg gac      240
Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
65                  70                  75                  80

cag gac ctc gtc ggc tgg cag gcg ccc ccc ggg gcg cgt tcc ttg aca      288
Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
                85                  90                  95

cca tgc acc tgt ggc agc tca gac ctt tac ttg gtc acg aga cat gct      336
Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
            100                 105                 110

gac gtc att ccg gtg cgc cgg cgg ggc gac agt agg ggg agc ctg ctc      384
Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
        115                 120                 125

tcc ccc agg cct gtc tcc tac ttg aag ggc tct tcg ggt ggt cca ctg      432
Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
    130                 135                 140

ctc tgc cct tcg ggg cac gct gtg ggc atc ttc cgg gct gcc gta tgc      480
Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
145                 150                 155                 160

acc cgg ggg gtt gcg aag gcg gtg gac ttt gtg ccc gta gag tcc atg      528
Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
                165                 170                 175

gaa act act atg cgg tct ccg gtc ttc acg gac aac tca tcc ccc ccg      576
Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
            180                 185                 190

gcc gta ccg cag tca ttt caa gtg gcc cac cta cac gct ccc act ggc      624
Ala Val Pro Gln Ser Phe Gln Val Ala His Leu His Ala Pro Thr Gly
        195                 200                 205

agc ggc aag agt act aaa gtg ccg gct gca tat gca gcc caa ggg tac      672
Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
    210                 215                 220

aag gtg ctc gtc ctc aat ccg tcc gtt gcc gct acc tta ggg ttt ggg      720
Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
225                 230                 235                 240

gcg tat atg tct aag gca cac ggt att gac ccc aac atc aga act ggg      768
Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
                245                 250                 255
```

gta agg acc att acc aca ggc gcc ccc gtc aca tac tct acc tat ggc 816
Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
260 265 270

aag ttt ctt gcc gat ggt ggt tgc tct ggg ggc gct tat gac atc ata 864
Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
275 280 285

ata tgt gat gag tgc cat tca act gac tcg act aca atc ttg ggc atc 912
Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
290 295 300

ggc aca gtc ctg gac caa gcg gag acg gct gga gcg cgg ctt gtc gtg 960
Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
305 310 315 320

ctc gcc acc gct acg cct ccg gga tcg gtc acc gtg cca cac cca aac 1008
Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
325 330 335

atc gag gag gtg gcc ctg tct aat act gga gag atc ccc ttc tat ggc 1056
Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
340 345 350

aaa gcc atc ccc att gaa gcc atc agg ggg gga agg cat ctc att ttc 1104
Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
355 360 365

tgt cat tcc aag aag aag tgc gac gag ctc gcc gca aag ctg tca ggc 1152
Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
370 375 380

ctc gga atc aac gct gtg gcg tat tac cgg ggg ctc gat gtg tcc gtc 1200
Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
385 390 395 400

ata cca act atc gga gac gtc gtt gtc gtg gca aca gac gct ctg atg 1248
Ile Pro Thr Ile Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met
405 410 415

acg ggc tat acg ggc gac ttt gac tca gtg atc gac tgt aac aca tgt 1296
Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys
420 425 430

gtc acc cag aca gtc gac ttc agc ttg gat ccc acc ttc acc att gag 1344
Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu
435 440 445

acg acg acc gtg cct caa gac gca gtg tcg cgc tcg cag cgg cgg ggt 1392
Thr Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly
450 455 460

agg act ggc agg ggt agg aga ggc atc tac agg ttt gtg act ccg gga 1440
Arg Thr Gly Arg Gly Arg Arg Gly Ile Tyr Arg Phe Val Thr Pro Gly
465 470 475 480

```
gaa cgg ccc tcg ggc atg ttc gat tcc tcg gtc ctg tgt gag tgc tat      1488
Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr
                485                 490                 495

gac gcg ggc tgt gct tgg tac gag ctc acc ccc gcc gag acc tcg gtt      1536
Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Ser Val
            500                 505                 510

agg ttg cgg gcc tac ctg aac aca cca ggg ttg ccc gtt tgc cag gac      1584
Arg Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln Asp
        515                 520                 525

cac ctg gag ttc tgg gag agt gtc ttc aca ggc ctc acc cac ata gat      1632
His Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp
    530                 535                 540

gca cac ttc ttg tcc cag acc aag cag gca gga gac aac ttc ccc tac      1680
Ala His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr
545                 550                 555                 560

ctg gta gca tac caa gcc acg gtg tgc gcc agg gct cag gcc cca cct      1728
Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro
                565                 570                 575

cca tca tgg gat caa atg tgg aag tgt ctc ata cgg ctg aaa cct acg      1776
Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr
            580                 585                 590

ctg cac ggg cca aca ccc ttg ctg tac agg ctg gga gcc gtc caa aat      1824
Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn
        595                 600                 605

gag gtc acc ctc acc cac ccc ata acc aaa tac atc atg gca tgc atg      1872
Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met
    610                 615                 620

tcg gct gac ctg gag gtc gtc act agc acc tgg gtg ctg gtg ggc gga      1920
Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly
625                 630                 635                 640

gtc ctt gca gct ctg gcc gcg tat tgc ctg aca aca ggc agt gtg gtc      1968
Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val Val
                645                 650                 655

att gtg ggt agg att atc ttg tcc ggg agg ccg gct att gtt ccc gac      2016
Ile Val Gly Arg Ile Ile Leu Ser Gly Arg Pro Ala Ile Val Pro Asp
            660                 665                 670

agg gag ttt ctc tac cag gag ttc gat gaa atg gaa gag tgc gcc tcg      2064
Arg Glu Phe Leu Tyr Gln Glu Phe Asp Glu Met Glu Glu Cys Ala Ser
        675                 680                 685

cac ctc cct tac atc gag cag gga atg cag ctc gcc gag caa ttc aag      2112
```

His Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe Lys
690 695 700

cag aaa gcg ctc ggg tta ctg caa aca gcc acc aaa caa gcg gag gct 2160
Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu Ala
705 710 715 720

gct gct ccc gtg gtg gag tcc aag tgg cga gcc ctt gag aca ttc tgg 2208
Ala Ala Pro Val Val Glu Ser Lys Trp Arg Ala Leu Glu Thr Phe Trp
725 730 735

gcg aag cac atg tgg aat ttc atc agc ggg ata cag tac tta gca ggc 2256
Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly
740 745 750

tta tcc act ctg cct ggg aac ccc gca ata gca tca ttg atg gca ttc 2304
Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe
755 760 765

aca gcc tct atc acc agc ccg ctc acc acc caa agt acc ctc ctg ttt 2352
Thr Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Ser Thr Leu Leu Phe
770 775 780

aac atc ttg ggg ggg tgg gtg gct gcc caa ctc gcc ccc ccc agc gcc 2400
Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser Ala
785 790 795 800

gct tcg gct ttc gtg ggc gcc ggc atc gcc ggt gcg gct gtt ggc agc 2448
Ala Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Val Gly Ser
805 810 815

ata ggc ctt ggg aag gtg ctt gtg gac att ctg gcg ggt tat gga gca 2496
Ile Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly Ala
820 825 830

gga gtg gcc ggc gcg ctc gtg gcc ttc aag gtc atg agc ggc gag atg 2544
Gly Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu Met
835 840 845

ccc tcc acc gag gac ctg gtc aat cta ctt cct gcc atc ctc tct cct 2592
Pro Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro
850 855 860

ggc gcc ctg gtc gtc ggg gtc gtg tgt gca gca ata ctg cgt cga cac 2640
Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His
865 870 875 880

gtg ggt ccg gga gag ggg gct gtg cag tgg atg aac cgg ctg ata gcg 2688
Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala
885 890 895

ttc gcc tcg cgg ggt aat cat gtt tcc ccc acg cac tat gtg cct gag 2736
Phe Ala Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu
900 905 910

```
agc gac gcc gca gcg cgt gtt act cag atc ctc tcc agc ctt acc atc      2784
Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr Ile
        915                 920                 925

act cag ctg ctg aaa agg ctc cac cag tgg att aat gaa gac tgc tcc      2832
Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys Ser
    930                 935                 940

aca ccg tgt tcc ggc tcg tgg cta agg gat gtt tgg gac tgg ata tgc      2880
Thr Pro Cys Ser Gly Ser Trp Leu Arg Asp Val Trp Asp Trp Ile Cys
945                 950                 955                 960

acg gtg ttg act gac ttc aag acc tgg ctc cag tcc aag ctc ctg ccg      2928
Thr Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu Pro
                965                 970                 975

cag cta ccg gga gtc cct ttt ttc tcg tgc caa cgc ggg tac aag gga      2976
Gln Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys Gly
            980                 985                 990

gtc tgg cgg gga gac ggc atc atg caa acc acc tgc cca tgt gga gca      3024
Val Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly Ala
        995                 1000                1005

cag atc acc gga cat gtc aaa aac ggt tcc atg agg atc gtc ggg cct      3072
Gln Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly Pro
    1010                1015                1020

aag acc tgc agc aac acg tgg cat gga aca ttc ccc atc aac gca tac      3120
Lys Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala Tyr
1025                1030                1035                1040

acc acg ggc ccc tgc aca ccc tct cca gcg cca aac tat tct agg gcg      3168
Thr Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg Ala
                1045                1050                1055

ctg tgg cgg gtg gcc gct gag gag tac gtg gag gtc acg cgg gtg ggg      3216
Leu Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Val Thr Arg Val Gly
            1060                1065                1070

gat ttc cac tac gtg acg ggc atg acc act gac aac gta aag tgc cca      3264
Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys Pro
        1075                1080                1085

tgc cag gtt ccg gct cct gaa ttc ttc acg gag gtg gac gga gtg cgg      3312
Cys Gln Val Pro Ala Pro Glu Phe Phe Thr Glu Val Asp Gly Val Arg
    1090                1095                1100

ttg cac agg tac gct ccg gcg tgc agg cct ctc cta cgg gag gag gtt      3360
Leu His Arg Tyr Ala Pro Ala Cys Arg Pro Leu Leu Arg Glu Glu Val
1105                1110                1115                1120

aca ttc cag gtc ggg ctc aac caa tac ctg gtt ggg tca cag cta cca      3408
Thr Phe Gln Val Gly Leu Asn Gln Tyr Leu Val Gly Ser Gln Leu Pro
                1125                1130                1135
```

```
tgc gag ccc gaa ccg gat gta gca gtg ctc act tcc atg ctc acc gac      3456
Cys Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp
            1140                1145                1150

ccc tcc cac atc aca gca gaa acg gct aag cgt agg ttg gcc agg ggg      3504
Pro Ser His Ile Thr Ala Glu Thr Ala Lys Arg Arg Leu Ala Arg Gly
        1155                1160                1165

tct ccc ccc tcc ttg gcc agc tct tca gct agc cag ttg tct gcg cct      3552
Ser Pro Pro Ser Leu Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro
    1170                1175                1180

tcc ttg aag gcg aca tgc act acc cac cat gtc tct ccg gac gct gac      3600
Ser Leu Lys Ala Thr Cys Thr Thr His His Val Ser Pro Asp Ala Asp
1185                1190                1195                1200

ctc atc gag gcc aac ctc ctg tgg cgg cag gag atg ggc ggg aac atc      3648
Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile
                1205                1210                1215

acc cgc gtg gag tcg gag aac aag gtg gta gtc ctg gac tct ttc gac      3696
Thr Arg Val Glu Ser Glu Asn Lys Val Val Val Leu Asp Ser Phe Asp
            1220                1225                1230

ccg ctt cga gcg gag gag gat gag agg gaa gta tcc gtt ccg gcg gag      3744
Pro Leu Arg Ala Glu Glu Asp Glu Arg Glu Val Ser Val Pro Ala Glu
        1235                1240                1245

atc ctg cgg aaa tcc aag aag ttc ccc gca gcg atg ccc atc tgg gcg      3792
Ile Leu Arg Lys Ser Lys Lys Phe Pro Ala Ala Met Pro Ile Trp Ala
    1250                1255                1260

cgc ccg gat tac aac cct cca ctg tta gag tcc tgg aag gac ccg gac      3840
Arg Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp
1265                1270                1275                1280

tac gtc cct ccg gtg gtg cac ggg tgc ccg ttg cca cct atc aag gcc      3888
Tyr Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala
                1285                1290                1295

cct cca ata cca cct cca cgg aga aag agg acg gtt gtc cta aca gag      3936
Pro Pro Ile Pro Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu
            1300                1305                1310

tcc tcc gtg tct tct gcc tta gcg gag ctc gct act aag acc ttc ggc      3984
Ser Ser Val Ser Ser Ala Leu Ala Glu Leu Ala Thr Lys Thr Phe Gly
        1315                1320                1325

agc tcc gaa tca tcg gcc gtc gac agc ggc acg gcg acc gcc ctt cct      4032
Ser Ser Glu Ser Ser Ala Val Asp Ser Gly Thr Ala Thr Ala Leu Pro
    1330                1335                1340

gac cag gcc tcc gac gac ggt gac aaa gga tcc gac gtt gag tcg tac      4080
```

```
Asp Gln Ala Ser Asp Asp Gly Asp Lys Gly Ser Asp Val Glu Ser Tyr
1345                1350                1355                1360

tcc tcc atg ccc ccc ctt gag ggg gaa ccg ggg gac ccc gat ctc agt      4128
Ser Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser
                1365                1370                1375

gac ggg tct tgg tct acc gtg agc gag gaa gct agt gag gat gtc gtc      4176
Asp Gly Ser Trp Ser Thr Val Ser Glu Glu Ala Ser Glu Asp Val Val
            1380                1385                1390

tgc tgc tca atg tcc tac aca tgg aca ggc gcc ttg atc acg cca tgc      4224
Cys Cys Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr Pro Cys
        1395                1400                1405

gct gcg gag gaa agc aag ctg ccc atc aac gcg ttg agc aac tct ttg      4272
Ala Ala Glu Glu Ser Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu
    1410                1415                1420

ctg cgc cac cat aac atg gtt tat gcc aca aca tct cgc agc gca ggc      4320
Leu Arg His His Asn Met Val Tyr Ala Thr Thr Ser Arg Ser Ala Gly
1425                1430                1435                1440

ctg cgg cag aag aag gtc acc ttt gac aga ctg caa gtc ctg gac gac      4368
Leu Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Asp
                1445                1450                1455

cac tac cgg gac gtg ctc aag gag atg aag gcg aag gcg tcc aca gtt      4416
His Tyr Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser Thr Val
            1460                1465                1470

aag gct aaa ctc cta tcc gta gag gaa gcc tgc aag ctg acg ccc cca      4464
Lys Ala Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr Pro Pro
        1475                1480                1485

cat tcg gcc aaa tcc aag ttt ggc tat ggg gca aag gac gtc cgg aac      4512
His Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Asn
    1490                1495                1500

cta tcc agc aag gcc gtt aac cac atc cac tcc gtg tgg aag gac ttg      4560
Leu Ser Ser Lys Ala Val Asn His Ile His Ser Val Trp Lys Asp Leu
1505                1510                1515                1520

ctg gaa gac act gtg aca cca att gac acc acc atc atg gca aaa aat      4608
Leu Glu Asp Thr Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn
                1525                1530                1535

gag gtt ttc tgt gtc caa cca gag aaa gga ggc cgt aag cca gcc cgc      4656
Glu Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg
            1540                1545                1550

ctt atc gta ttc cca gat ctg gga gtc cgt gta tgc gag aag atg gcc      4704
Leu Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala
        1555                1560                1565
```

```
ctc tat gat gtg gtc tcc acc ctt cct cag gtc gtg atg ggc tcc tca      4752
Leu Tyr Asp Val Val Ser Thr Leu Pro Gln Val Val Met Gly Ser Ser
    1570                1575                1580

tac gga ttc cag tac tct cct ggg cag cga gtc gag ttc ctg gtg aat      4800
Tyr Gly Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn
1585                1590                1595                1600

acc tgg aaa tca aag aaa aac ccc atg ggc ttt tca tat gac act cgc      4848
Thr Trp Lys Ser Lys Lys Asn Pro Met Gly Phe Ser Tyr Asp Thr Arg
                1605                1610                1615

tgt ttc gac tca acg gtc acc gag aac gac atc cgt gtt gag gag tca      4896
Cys Phe Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser
            1620                1625                1630

att tac caa tgt tgt gac ttg gcc ccc gaa gcc aga cag gcc ata aaa      4944
Ile Tyr Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys
        1635                1640                1645

tcg ctc aca gag cgg ctt tat atc ggg ggt cct ctg act aat tca aaa      4992
Ser Leu Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys
    1650                1655                1660

ggg cag aac tgc ggt tat cgc cgg tgc cgc gcg agc ggc gtg ctg acg      5040
Gly Gln Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr
1665                1670                1675                1680

act agc tgc ggt aac acc ctc aca tgt tac ttg aag gcc tct gca gcc      5088
Thr Ser Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala
                1685                1690                1695

tgt cga gct gcg aag ctc cag gac tgc acg atg ctc gtg aac gga gac      5136
Cys Arg Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp
            1700                1705                1710

gac ctt gtc gtt atc tgt gaa agc gcg gga acc caa gag gac gcg gcg      5184
Asp Leu Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala
        1715                1720                1725

agc cta cga gtc ttc acg gag gct atg act agg tac tct gcc ccc ccc      5232
Ser Leu Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro
    1730                1735                1740

ggg gac ccg ccc caa cca gaa tac gac ttg gag ctg ata aca tca tgt      5280
Gly Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys
1745                1750                1755                1760

tcc tcc aat gtg tcg gtc gcc cac gat gca tca ggc aaa agg gtg tac      5328
Ser Ser Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr
                1765                1770                1775

tac ctc acc cgt gat ccc acc acc ccc ctc gca cgg gct gcg tgg gaa      5376
Tyr Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu
            1780                1785                1790
```

```
aca gct aga cac act cca gtt aac tcc tgg cta ggc aac att atc atg      5424
Thr Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met
        1795                1800                1805

tat gcg ccc act ttg tgg gca agg atg att ctg atg act cac ttc ttc      5472
Tyr Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe
    1810                1815                1820

tcc atc ctt cta gca cag gag caa ctt gaa aaa gcc ctg gac tgc cag      5520
Ser Ile Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln
1825                1830                1835                1840

atc tac ggg gcc tgt tac tcc att gag cca ctt gac cta cct cag atc      5568
Ile Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile
                1845                1850                1855

att gaa cga ctc cat ggc ctt agc gca ttt tca ctc cat agt tac tct      5616
Ile Glu Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser
            1860                1865                1870

cca ggt gag atc aat agg gtg gct tca tgc ctc agg aaa ctt ggg gta      5664
Pro Gly Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val
        1875                1880                1885

cca ccc ttg cga gtc tgg aga cat cgg gcc agg agc gtc cgc gct agg      5712
Pro Pro Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg
    1890                1895                1900

cta ctg tcc cag ggg ggg agg gcc gcc act tgt ggc aag tac ctc ttc      5760
Leu Leu Ser Gln Gly Gly Arg Ala Ala Thr Cys Gly Lys Tyr Leu Phe
1905                1910                1915                1920

aac tgg gca gtg aag acc aaa ctc aaa ctc act cca atc ccg gct gcg      5808
Asn Trp Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Ile Pro Ala Ala
                1925                1930                1935

tcc cag ctg gac ttg tcc ggc tgg ttc gtt gct ggt tac agc ggg gga      5856
Ser Gln Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Ser Gly Gly
            1940                1945                1950

gac ata tat cac agc ctg tct cgt gcc cga ccc cgc tgg ttc atg ctg      5904
Asp Ile Tyr His Ser Leu Ser Arg Ala Arg Pro Arg Trp Phe Met Leu
        1955                1960                1965

tgc cta ctc cta ctt tct gta ggg gta ggc atc tac ctg ctc ccc aac      5952
Cys Leu Leu Leu Leu Ser Val Gly Val Gly Ile Tyr Leu Leu Pro Asn
    1970                1975                1980

cga                                                                  5955
Arg
1985
```

<210> 6
<211> 1984

<212> PRT
<213> Artificial Sequence

<220>
<223> NS sequence

<400> 6
Ala Pro Ile Thr Ala Tyr Ser Gln Gln Thr Arg Gly Leu Leu Gly Cys
1 5 10 15
Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly Glu
20 25 30
Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys Val
35 40 45
Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr Leu
50 55 60
Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp Gln
65 70 75 80
Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr Pro
85 90 95
Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp
100 105 110
Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu Ser
115 120 125
Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu Leu
130 135 140
Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys Thr
145 150 155 160
Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met Glu
165 170 175
Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro Ala
180 185 190
Val Pro Gln Ser Phe Gln Val Ala His Leu His Ala Pro Thr Gly Ser
195 200 205
Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr Lys
210 215 220
Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly Ala
225 230 235 240
Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly Val
245 250 255
Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly Lys
260 265 270
Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile
275 280 285
Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile Gly
290 295 300
Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu
305 310 315 320
Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn Ile
325 330 335
Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly Lys
340 345 350
Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe Cys
355 360 365
His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly Leu
370 375 380

```
Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile
385                 390                 395                 400
Pro Thr Ile Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met Thr
                405                 410                 415
Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys Val
            420                 425                 430
Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr
        435                 440                 445
Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly Arg
    450                 455                 460
Thr Gly Arg Gly Arg Arg Gly Ile Tyr Arg Phe Val Thr Pro Gly Glu
465                 470                 475                 480
Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp
                485                 490                 495
Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Ser Val Arg
            500                 505                 510
Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln Asp His
        515                 520                 525
Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp Ala
    530                 535                 540
His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr Leu
545                 550                 555                 560
Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro
                565                 570                 575
Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu
            580                 585                 590
His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu
        595                 600                 605
Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met Ser
    610                 615                 620
Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly Val
625                 630                 635                 640
Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val Val Ile
                645                 650                 655
Val Gly Arg Ile Ile Leu Ser Gly Arg Pro Ala Ile Val Pro Asp Arg
            660                 665                 670
Glu Phe Leu Tyr Gln Glu Phe Asp Glu Met Glu Glu Cys Ala Ser His
        675                 680                 685
Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe Lys Gln
    690                 695                 700
Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu Ala Ala
705                 710                 715                 720
Ala Pro Val Val Glu Ser Lys Trp Arg Ala Leu Glu Thr Phe Trp Ala
                725                 730                 735
Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu
            740                 745                 750
Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe Thr
        755                 760                 765
Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Ser Thr Leu Leu Phe Asn
    770                 775                 780
Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser Ala Ala
785                 790                 795                 800
Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Val Gly Ser Ile
                805                 810                 815
Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly Ala Gly
```

```
            820                 825                 830
Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu Met Pro
        835                 840                 845
Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly
    850                 855                 860
Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His Val
865                 870                 875                 880
Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala Phe
                885                 890                 895
Ala Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu Ser
            900                 905                 910
Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr Ile Thr
        915                 920                 925
Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys Ser Thr
    930                 935                 940
Pro Cys Ser Gly Ser Trp Leu Arg Asp Val Trp Asp Trp Ile Cys Thr
945                 950                 955                 960
Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu Pro Gln
                965                 970                 975
Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys Gly Val
            980                 985                 990
Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly Ala Gln
        995                 1000                1005
Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly Pro Lys
    1010                1015                1020
Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala Tyr Thr
1025                1030                1035                1040
Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg Ala Leu
                1045                1050                1055
Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Val Thr Arg Val Gly Asp
            1060                1065                1070
Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys Pro Cys
        1075                1080                1085
Gln Val Pro Ala Pro Glu Phe Phe Thr Glu Val Asp Gly Val Arg Leu
    1090                1095                1100
His Arg Tyr Ala Pro Ala Cys Arg Pro Leu Leu Arg Glu Glu Val Thr
1105                1110                1115                1120
Phe Gln Val Gly Leu Asn Gln Tyr Leu Val Gly Ser Gln Leu Pro Cys
                1125                1130                1135
Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp Pro
            1140                1145                1150
Ser His Ile Thr Ala Glu Thr Ala Lys Arg Arg Leu Ala Arg Gly Ser
        1155                1160                1165
Pro Pro Ser Leu Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser
    1170                1175                1180
Leu Lys Ala Thr Cys Thr Thr His His Val Ser Pro Asp Ala Asp Leu
1185                1190                1195                1200
Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile Thr
                1205                1210                1215
Arg Val Glu Ser Glu Asn Lys Val Val Val Leu Asp Ser Phe Asp Pro
            1220                1225                1230
Leu Arg Ala Glu Glu Asp Glu Arg Glu Val Ser Val Pro Ala Glu Ile
        1235                1240                1245
Leu Arg Lys Ser Lys Lys Phe Pro Ala Ala Met Pro Ile Trp Ala Arg
    1250                1255                1260
```

```
Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp Tyr
1265                1270                1275                1280
Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala Pro
                1285                1290                1295
Pro Ile Pro Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu Ser
            1300                1305                1310
Ser Val Ser Ser Ala Leu Ala Glu Leu Ala Thr Lys Thr Phe Gly Ser
        1315                1320                1325
Ser Glu Ser Ser Ala Val Asp Ser Gly Thr Ala Thr Ala Leu Pro Asp
    1330                1335                1340
Gln Ala Ser Asp Asp Gly Asp Lys Gly Ser Asp Val Glu Ser Tyr Ser
1345                1350                1355                1360
Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp
                1365                1370                1375
Gly Ser Trp Ser Thr Val Ser Glu Glu Ala Ser Glu Asp Val Val Cys
            1380                1385                1390
Cys Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr Pro Cys Ala
        1395                1400                1405
Ala Glu Glu Ser Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu
    1410                1415                1420
Arg His His Asn Met Val Tyr Ala Thr Thr Ser Arg Ser Ala Gly Leu
1425                1430                1435                1440
Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Asp His
                1445                1450                1455
Tyr Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser Thr Val Lys
            1460                1465                1470
Ala Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr Pro Pro His
        1475                1480                1485
Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Asn Leu
    1490                1495                1500
Ser Ser Lys Ala Val Asn His Ile His Ser Val Trp Lys Asp Leu Leu
1505                1510                1515                1520
Glu Asp Thr Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu
                1525                1530                1535
Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu
            1540                1545                1550
Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu
        1555                1560                1565
Tyr Asp Val Val Ser Thr Leu Pro Gln Val Val Met Gly Ser Ser Tyr
    1570                1575                1580
Gly Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn Thr
1585                1590                1595                1600
Trp Lys Ser Lys Lys Asn Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys
                1605                1610                1615
Phe Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile
            1620                1625                1630
Tyr Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser
        1635                1640                1645
Leu Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly
    1650                1655                1660
Gln Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr
1665                1670                1675                1680
Ser Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys
                1685                1690                1695
```

```
Arg Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp Asp
            1700                1705                1710
Leu Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser
        1715                1720                1725
Leu Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly
    1730                1735                1740
Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser
1745                1750                1755                1760
Ser Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr Tyr
                1765                1770                1775
Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr
            1780                1785                1790
Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr
        1795                1800                1805
Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser
    1810                1815                1820
Ile Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln Ile
1825                1830                1835                1840
Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile
                1845                1850                1855
Glu Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro
            1860                1865                1870
Gly Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val Pro
        1875                1880                1885
Pro Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu
    1890                1895                1900
Leu Ser Gln Gly Gly Arg Ala Ala Thr Cys Gly Lys Tyr Leu Phe Asn
1905                1910                1915                1920
Trp Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Ile Pro Ala Ala Ser
                1925                1930                1935
Gln Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Ser Gly Gly Asp
            1940                1945                1950
Ile Tyr His Ser Leu Ser Arg Ala Arg Pro Arg Trp Phe Met Leu Cys
        1955                1960                1965
Leu Leu Leu Leu Ser Val Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg
    1970                1975                1980
```

<210> 7
<211> 4909
<212> DNA
<213> Artificial Sequence

<220>
<223> pV1J nucleic acid

<400> 7

```
tcgcgcgttt cggtgatgac ggtgaaaacc tctgacacat gcagctcccg gagacggtca      60
cagcttgtct gtaagcggat gccgggagca gacaagcccg tcagggcgcg tcagcgggtg     120
ttggcgggtg tcggggctgg cttaactatg cggcatcaga gcagattgta ctgagagtgc     180
accatatgcg gtgtgaaata ccgcacagat gcgtaaggag aaaataccgc atcagattgg     240
ctattggcca ttgcatacgt tgtatccata tcataatatg tacatttata ttggctcatg     300
tccaacatta ccgccatgtt gacattgatt attgactagt tattaatagt aatcaattac     360
ggggtcatta gttcatagcc catatatgga gttccgcgtt acataactta cggtaaatgg     420
cccgcctggc tgaccgccca acgacccccg cccattgacg tcaataatga cgtatgttcc     480
catagtaacg ccaataggga ctttccattg acgtcaatgg gtggagtatt tacggtaaac     540
```

```
tgcccacttg gcagtacatc aagtgtatca tatgccaagt acgcccccta ttgacgtcaa   600
tgacggtaaa tggcccgcct ggcattatgc ccagtacatg accttatggg actttcctac   660
ttggcagtac atctacgtat tagtcatcgc tattaccatg gtgatgcggt tttggcagta   720
catcaatggg cgtggatagc ggtttgactc acggggattt ccaagtctcc accccattga   780
cgtcaatggg agtttgtttt ggcaccaaaa tcaacgggac tttccaaaat gtcgtaacaa   840
ctccgcccca ttgacgcaaa tgggcggtag gcgtgtacgg tgggaggtct atataagcag   900
agctcgttta gtgaaccgtc agatcgcctg gagacgccat ccacgctgtt ttgacctcca   960
tagaagacac cgggaccgat ccagcctccg cggccgggaa cggtgcattg gaacgcggat  1020
tccccgtgcc aagagtgacg taagtaccgc ctatagactc tataggcaca cccctttggc  1080
tcttatgcat gctatactgt ttttggcttg gggcctatac acccccgctt ccttatgcta  1140
taggtgatgg tatagcttag cctataggtg tgggttattg accattattg accactcccc  1200
tattggtgac gatactttcc attactaatc cataacatgg ctctttgcca caactatctc  1260
tattggctat atgccaatac tctgtccttc agagactgac acggactctg tatttttaca  1320
ggatggggtc ccatttatta tttacaaatt cacatataca acaacgccgt cccccgtgcc  1380
cgcagttttt attaaacata gcgtgggatc tccacgcgaa tctcgggtac gtgttccgga  1440
catgggctct tctccggtag cggcggagct tccacatccg agccctggtc ccatgcctcc  1500
agcggctcat ggtcgctcgg cagctccttg ctcctaacag tggaggccag acttaggcac  1560
agcacaatgc ccaccaccac cagtgtgccg cacaaggccg tggcggtagg gtatgtgtct  1620
gaaaatgagc gtggagattg ggctcgcacg gctgacgcag atggaagact taaggcagcg  1680
gcagaagaag atgcaggcag ctgagttgtt gtattctgat aagagtcaga ggtaactccc  1740
gttgcggtgc tgttaacggt ggagggcagt gtagtctgag cagtactcgt tgctgccgcg  1800
cgcgccacca gacataatag ctgacagact aacagactgt tcctttccat gggtcttttc  1860
tgcagtcacc gtccttagat ctaggtacca gatatcagaa ttcagtcgac agcggccgcg  1920
atctgctgtg ccttctagtt gccagccatc tgttgtttgc ccctcccccg tgccttcctt  1980
gaccctggaa ggtgccactc ccactgtcct ttcctaataa aatgaggaaa ttgcatcgca  2040
ttgtctgagt aggtgtcatt ctattctggg gggtggggtg gggcaggaca gcaaggggga  2100
ggattgggaa gacaatagca ggcatgctgg ggatgcggtg ggctctatgg ccgctgcggc  2160
caggtgctga agaattgacc cggttcctcc tgggccagaa agaagcaggc acatcccctt  2220
ctctgtgaca caccctgtcc acgcccctgg ttcttagttc cagccccact cataggacac  2280
tcatagctca ggagggctcc gccttcaatc ccacccgcta aagtacttgg agcggtctct  2340
ccctccctca tcagcccacc aaaccaaacc tagcctccaa gagtgggaag aaattaaagc  2400
aagataggct attaagtgca gagggagaga aaatgcctcc aacatgtgag gaagtaatga  2460
gagaaatcat agaatttctt ccgcttcctc gctcactgac tcgctgcgct cggtcgttcg  2520
gctgcggcga gcggtatcag ctcactcaaa ggcggtaata cggttatcca cagaatcagg  2580
ggataacgca ggaaagaaca tgtgagcaaa aggccagcaa aaggccagga accgtaaaaa  2640
ggccgcgttg ctggcgtttt tccataggct ccgcccccct gacgagcatc acaaaaatcg  2700
acgctcaagt cagaggtggc gaaacccgac aggactataa agataccagg cgtttccccc  2760
tggaagctcc ctcgtgcgct ctcctgttcc gaccctgccg cttaccggat acctgtccgc  2820
ctttctccct tcgggaagcg tggcgctttc tcatagctca cgctgtaggt atctcagttc  2880
ggtgtaggtc gttcgctcca agctgggctg tgtgcacgaa ccccccgttc agcccgaccg  2940
ctgcgcctta tccggtaact atcgtcttga gtccaacccg gtaagacacg acttatcgcc  3000
actggcagca gccactggta acaggattag cagagcgagg tatgtaggcg gtgctacaga  3060
gttcttgaag tggtggccta actacggcta cactagaaga acagtatttg gtatctgcgc  3120
tctgctgaag ccagttacct tcggaaaaag agttggtagc tcttgatccg gcaaacaaac  3180
caccgctggt agcggtggtt tttttgtttg caagcagcag attacgcgca gaaaaaaagg  3240
atctcaagaa gatcctttga tcttttctac ggggtctgac gctcagtgga acgaaaactc  3300
acgttaaggg attttggtca tgagattatc aaaaaggatc ttcacctaga tccttttaaa  3360
ttaaaaatga agttttaaat caatctaaag tatatatgag taaacttggt ctgacagtta  3420
ccaatgctta atcagtgagg cacctatctc agcgatctgt ctatttcgtt catccatagt  3480
tgcctgactc gggggggggg ggcgctgagg tctgcctcgt gaagaaggtg ttgctgactc  3540
ataccaggcc tgaatcgccc catcatccag ccagaaagtg agggagccac ggttgatgag  3600
agctttgttg taggtggacc agttggtgat tttgaacttt tgctttgcca cggaacggtc  3660
tgcgttgtcg ggaagatgcg tgatctgatc cttcaactca gcaaaagttc gatttattca  3720
acaaagccgc cgtcccgtca agtcagcgta atgctctgcc agtgttacaa ccaattaacc  3780
aattctgatt agaaaaactc atcgagcatc aaatgaaact gcaatttatt catatcagga  3840
```

ttatcaatac catatttttg aaaaagccgt ttctgtaatg aaggagaaaa ctcaccgagg 3900
cagttccata ggatggcaag atcctggtat cggtctgcga ttccgactcg tccaacatca 3960
atacaaccta ttaatttccc ctcgtcaaaa ataaggttat caagtgagaa atcaccatga 4020
gtgacgactg aatccggtga gaatggcaaa agcttatgca tttctttcca gacttgttca 4080
acaggccagc cattacgctc gtcatcaaaa tcactcgcat caaccaaacc gttattcatt 4140
cgtgattgcg cctgagcgag acgaaatacg cgatcgctgt taaaaggaca attacaaaca 4200
ggaatcgaat gcaaccggcg caggaacact gccagcgcat caacaatatt ttcacctgaa 4260
tcaggatatt cttctaatac ctggaatgct gttttcccgg ggatcgcagt ggtgagtaac 4320
catgcatcat caggagtacg gataaaatgc ttgatggtcg gaagaggcat aaattccgtc 4380
agccagttta gtctgaccat ctcatctgta acatcattgg caacgctacc tttgccatgt 4440
ttcagaaaca actctggcgc atcgggcttc ccatacaatc gatagattgt cgcacctgat 4500
tgcccgacat tatcgcgagc ccatttatac ccatataaat cagcatccat gttggaattt 4560
aatcgcggcc tcgagcaaga cgtttcccgt tgaatatggc tcataacacc ccttgtatta 4620
ctgtttatgt aagcagacag ttttattgtt catgatgata tatttttatc ttgtgcaatg 4680
taacatcaga gattttgaga cacaacgtgg ctttcccccc ccccccatta ttgaagcatt 4740
tatcagggtt attgtctcat gagcggatac atatttgaat gtatttagaa aaataaacaa 4800
ataggggttc cgcgcacatt tccccgaaaa gtgccacctg acgtctaaga aaccattatt 4860
atcatgacat taacctataa aaataggcgt atcacgaggc cctttcgtc 4909

<210> 8
<211> 35935
<212> DNA
<213> Adenovirus serotype 6

<400> 8
catcatcaat aatatacctt attttggatt gaagccaata tgataatgag ggggtggagt 60
ttgtgacgtg gcgcggggcg tgggaacggg gcgggtgacg tagtagtgtg gcggaagtgt 120
gatgttgcaa gtgtggcgga acacatgtaa gcgacggatg tggcaaaagt gacgtttttg 180
gtgtgcgccg gtgtacacag gaagtgacaa ttttcgcgcg gttttaggcg gatgttgtag 240
taaatttggg cgtaaccgag taagatttgg ccattttcgc gggaaaactg aataagagga 300
agtgaaatct gaataatttt gtgttactca tagcgcgtaa tatttgtcta gggccgcggg 360
gactttgacc gtttacgtgg agactcgccc aggtgttttt ctcaggtgtt ttccgcgttc 420
cgggtcaaag ttggcgtttt attattatag tcagctgacg tgtagtgtat ttatacccgg 480
tgagttcctc aagaggccac tcttgagtgc cagcgagtag agttttctcc tccgagccgc 540
tccgacaccg ggactgaaaa tgagacatat tatctgccac ggaggtgtta ttaccgaaga 600
aatggccgcc agtcttttgg accagctgat cgaagaggta ctggctgata atcttccacc 660
tcctagccat tttgaaccac ctacccttca cgaactgtat gatttagacg tgacggcccc 720
cgaagatccc aacgaggagg cggtttcgca gatttttccc gactctgtaa tgttggcggt 780
gcaggaaggg attgacttac tcacttttcc gccggcgccc ggttctccgg agccgcctca 840
cctttcccgg cagcccgagc agccggagca gagagccttg ggtccggttt ctatgccaaa 900
ccttgtaccg gaggtgatcg atcttacctg ccacgaggct ggctttccac ccagtgacga 960
cgaggatgaa gagggtgagg agtttgtgtt agattatgtg gagcaccccg ggcacggttg 1020
caggtcttgt cattatcacc ggaggaatac gggggaccca gatattatgt gttcgctttg 1080
ctatatgagg acctgtggca tgtttgtcta cagtaagtga aaattatggg cagtgggtga 1140
tagagtggtg ggtttggtgt ggtaattttt tttttaattt ttacagtttt gtggtttaaa 1200
gaattttgta ttgtgatttt tttaaaaggt cctgtgtctg aacctgagcc tgagcccgag 1260
ccagaaccgg agcctgcaag acctacccgc cgtcctaaaa tggcgcctgc tatcctgaga 1320
cgcccgacat cacctgtgtc tagagaatgc aatagtagta cggatagctg tgactccggt 1380
ccttctaaca cacctcctga gatacacccg gtggtcccgc tgtgccccat taaaccagtt 1440
gccgtgagag ttggtgggcg tcgccaggct gtggaatgta tcgaggactt gcttaacgag 1500
cctgggcaac ctttggactt gagctgtaaa cgccccaggc cataaggtgt aaacctgtga 1560
ttgcgtgtgt ggttaacgcc tttgtttgct gaatgagttg atgtaagttt aataaagggt 1620
gagataatgt ttaacttgca tggcgtgtta aatggggcgg ggcttaaagg gtatataatg 1680
cgccgtgggc taatcttggt tacatctgac ctcatggagg cttgggagtg tttggaagat 1740
ttttctgctg tgcgtaactt gctggaacag agctctaaca gtacctcttg gttttggagg 1800

tttctgtggg gctcatccca ggcaaagtta gtctgcagaa ttaaggagga ttacaagtgg 1860
gaatttgaag agcttttgaa atcctgtggt gagctgtttg attctttgaa tctgggtcac 1920
caggcgcttt tccaagagaa ggtcatcaag actttggatt tttccacacc ggggcgcgct 1980
gcggctgctg ttgctttttt gagttttata aaggataaat ggagcgaaga aacccatctg 2040
agcggggggt acctgctgga ttttctggcc atgcatctgt ggagagcggt tgtgagacac 2100
aagaatcgcc tgctactgtt gtcttccgtc cgcccggcga taataccgac ggaggagcag 2160
cagcagcagc aggaggaagc caggcggcgg cggcaggagc agagcccatg gaacccgaga 2220
gccggcctgg accctcggga atgaatgttg tacaggtggc tgaactgtat ccagaactga 2280
gacgcatttt gacaattaca gaggatgggc aggggctaaa gggggtaaag agggagcggg 2340
gggcttgtga ggctacagag gaggctagga atctagcttt tagcttaatg accagacacc 2400
gtcctgagtg tattactttt caacagatca aggataattg cgctaatgag cttgatctgc 2460
tggcgcagaa gtattccata gagcagctga ccacttactg gctgcagcca ggggatgatt 2520
ttgaggaggc tattagggta tatgcaaagg tggcacttag gccagattgc aagtacaaga 2580
tcagcaaact tgtaaatatc aggaattgtt gctacatttc tgggaacggg gccgaggtgg 2640
agatagatac ggaggatagg gtggccttta gatgtagcat gataaatatg tggccggggg 2700
tgcttggcat ggacggggtg gttattatga atgtaaggtt tactggcccc aattttagcg 2760
gtacggtttt cctggccaat accaacctta tcctacacgg tgtaagcttc tatgggttta 2820
acaatacctg tgtggaagcc tggaccgatg taagggttcg gggctgtgcc ttttactgct 2880
gctggaaggg ggtggtgtgt cgccccaaaa gcagggcttc aattaagaaa tgcctctttg 2940
aaaggtgtac cttgggtatc ctgtctgagg gtaactccag ggtgcgccac aatgtggcct 3000
ccgactgtgg ttgcttcatg ctagtgaaaa gcgtggctgt gattaagcat aacatggtat 3060
gtggcaactg cgaggacagg gcctctcaga tgctgacctg ctcggacggc aactgtcacc 3120
tgctgaagac cattcacgta gccagccact ctcgcaaggc ctggccagtg tttgagcata 3180
acatactgac ccgctgttcc ttgcatttgg gtaacaggag gggggtgttc ctaccttacc 3240
aatgcaattt gagtcacact aagatattgc ttgagcccga gagcatgtcc aaggtgaacc 3300
tgaacggggt gtttgacatg accatgaaga tctggaaggt gctgaggtac gatgagaccc 3360
gcaccaggtg cagaccctgc gagtgtggcg gtaaacatat taggaaccag cctgtgatgc 3420
tggatgtgac cgaggagctg aggcccgatc acttggtgct ggcctgcacc cgcgctgagt 3480
ttggctctag cgatgaagat acagattgag gtactgaaat gtgtgggcgt ggcttaaggg 3540
tgggaaagaa tatataaggt gggggtctta tgtagttttg tatctgtttt gcagcagccg 3600
ccgccgccat gagcaccaac tcgtttgatg gaagcattgt gagctcatat ttgacaacgc 3660
gcatgccccc atgggccggg gtgcgtcaga atgtgatggg ctccagcatt gatggtcgcc 3720
ccgtcctgcc cgcaaactct actaccttga cctacgagac cgtgtctgga acgccgttgg 3780
agactgcagc ctccgccgcc gcttcagccg ctgcagccac cgcccgcggg attgtgactg 3840
actttgcttt cctgagcccg cttgcaagca gtgcagcttc ccgttcatcc gcccgcgatg 3900
acaagttgac ggctcttttg gcacaattgg attctttgac ccgggaactt aatgtcgttt 3960
ctcagcagct gttggatctg cgccagcagg tttctgccct gaaggcttcc tcccctccca 4020
atgcggttta aaacataaat aaaaaaccag actctgtttg gatttggatc aagcaagtgt 4080
cttgctgtct ttatttaggg gttttgcgcg cgcggtaggc ccgggaccag cggtctcggt 4140
cgttgagggt cctgtgtatt ttttccagga cgtggtaaag gtgactctgg atgttcagat 4200
acatgggcat aagcccgtct ctggggtgga ggtagcacca ctgcagagct tcatgctgcg 4260
gggtggtgtt gtagatgatc cagtcgtagc aggagcgctg ggcgtggtgc ctaaaaatgt 4320
ctttcagtag caagctgatt gccaggggca ggcccttggt gtaagtgttt acaaagcggt 4380
taagctggga tgggtgcata cgtggggata tgagatgcat cttggactgt atttttaggt 4440
tggctatgtt cccagccata tccctccggg gattcatgtt gtgcagaacc accagcacag 4500
tgtatccggt gcacttggga aatttgtcat gtagcttaga aggaaatgcg tggaagaact 4560
tggagacgcc cttgtgacct ccaagatttt ccatgcattc gtccataatg atggcaatgg 4620
gcccacgggc ggcggcctgg gcgaagatat ttctgggatc actaacgtca tagttgtgtt 4680
ccaggatgag atcgtcatag gccattttta caaagcgcgg gcggagggtg ccagactgcg 4740
gtataatggt tccatccggc ccaggggcgt agttaccctc acagatttgc atttcccacg 4800
ctttgagttc agatgggggg atcatgtcta cctgcggggc gatgaagaaa acggtttccg 4860
gggtagggga gatcagctgg gaagaaagca ggttcctgag cagctgcgac ttaccgcagc 4920
cggtgggccc gtaaatcaca cctattaccg ggtgcaactg gtagttaaga gagctgcagc 4980
tgccgtcatc cctgagcagg ggggccactt cgttaagcat gtccctgact cgcatgtttt 5040
ccctgaccaa atccgccaga aggcgctcgc cgcccagcga tagcagttct tgcaaggaag 5100

caaagttttt caacggtttg agaccgtccg ccgtaggcat gcttttgagc gtttgaccaa 5160
gcagttccag gcggtcccac agctcggtca cctgctctac ggcatctcga tccagcatat 5220
ctcctcgttt cgcgggttgg ggcggctttc gctgtacggc agtagtcggt gctcgtccag 5280
acgggccagg gtcatgtctt tccacgggcg cagggtcctc gtcagcgtag tctgggtcac 5340
ggtgaagggg tgcgctccgg gctgcgcgct ggccagggtg cgcttgaggc tggtcctgct 5400
ggtgctgaag cgctgccggt cttcgccctg cgcgtcggcc aggtagcatt tgaccatggt 5460
gtcatagtcc agcccctccg cggcgtggcc cttggcgcgc agcttgccct tggaggaggc 5520
gccgcacgag gggcagtgca gacttttgag ggcgtagagc ttgggcgcga gaaataccga 5580
ttccggggag taggcatccg cgccgcaggc cccgcagacg gtctcgcatt ccacgagcca 5640
ggtgagctct ggccgttcgg ggtcaaaaac caggtttccc ccatgctttt tgatgcgttt 5700
cttacctctg gtttccatga gccggtgtcc acgctcggtg acgaaaaggc tgtccgtgtc 5760
cccgtataca gacttgagag gcctgtcctc gagcggtgtt ccgcggtcct cctcgtatag 5820
aaactcggac cactctgaga caaaggctcg cgtccaggcc agcacgaagg aggctaagtg 5880
ggaggggtag cggtcgttgt ccactagggg gtccactcgc tccagggtgt gaagacacat 5940
gtcgccctct tcggcatcaa ggaaggtgat tggtttgtag gtgtaggcca cgtgaccggg 6000
tgttcctgaa ggggggctat aaaagggggt gggggcgcgt tcgtcctcac tctcttccgc 6060
atcgctgtct gcgagggcca gctgttgggg tgagtactcc ctctgaaaag cgggcatgac 6120
ttctgcgcta agattgtcag tttccaaaaa cgaggaggat ttgatattca cctggcccgc 6180
ggtgatgcct ttgagggtgg ccgcatccat ctggtcagaa aagacaatct ttttgttgtc 6240
aagcttggtg gcaaacgacc cgtagagggc gttggacagc aacttggcga tggagcgcag 6300
ggtttggttt ttgtcgcgat cggcgcgctc cttggccgcg atgtttagct gcacgtattc 6360
gcgcgcaacg caccgccatt cgggaaagac ggtggtgcgc tcgtcgggca ccaggtgcac 6420
gcgccaaccg cggttgtgca gggtgacaag gtcaacgctg gtggctacct ctccgcgtag 6480
gcgctcgttg gtccagcaga ggcggccgcc cttgcgcgag cagaatggcg gtagggggtc 6540
tagctgcgtc tcgtccgggg ggtctgcgtc cacggtaaag accccgggca gcaggcgcgc 6600
gtcgaagtag tctatcttgc atccttgcaa gtctagcgcc tgctgccatg cgcgggcggc 6660
aagcgcgcgc tcgtatgggt tgagtggggg accccatggc atggggtggg tgagcgcgga 6720
ggcgtacatg ccgcaaatgt cgtaaacgta gaggggctct ctgagtattc caagatatgt 6780
agggtagcat cttccaccgc ggatgctggc gcgcacgtaa tcgtatagtt cgtgcgaggg 6840
agcgaggagg tcgggaccga ggttgctacg ggcgggctgc tctgctcgga agactatctg 6900
cctgaagatg gcatgtgagt tggatgatat ggttggacgc tggaagacgt tgaagctggc 6960
gtctgtgaga cctaccgcgt cacgcacgaa ggaggcgtag gagtcgcgca gcttgttgac 7020
cagctcggcg gtgacctgca cgtctagggc gcagtagtcc agggtttcct tgatgatgtc 7080
atacttatcc tgtccctttt ttttccacag ctcgcggttg aggacaaact cttcgcggtc 7140
tttccagtac tcttggatcg gaaacccgtc ggcctccgaa cggtaagagc ctagcatgta 7200
gaactggttg acggcctggt aggcgcagca tccctttict acgggtagcg cgtatgcctg 7260
cgcggccttc cggagcgagg tgtgggtgag cgcaaaggtg tccctgacca tgactttgag 7320
gtactggtat ttgaagtcag tgtcgtcgca tccgccctgc tcccagagca aaaagtccgt 7380
gcgctttttg gaacgcggat ttggcagggc gaaggtgaca tcgttgaaga gtatctttcc 7440
cgcgcgaggc ataaagttgc gtgtgatgcg gaagggtccc ggcacctcgg aacggttgtt 7500
aattacctgg gcggcgagca cgatctcgtc aaagccgttg atgttgtggc ccacaatgta 7560
aagttccaag aagcgcggga tgcccttgat ggaaggcaat ttttaagtt cctcgtaggt 7620
gagctcttca ggggagctga gcccgtgctc tgaaagggcc cagtctgcaa gatgagggtt 7680
ggaagcgacg aatgagctcc acaggtcacg ggccattagc atttgcaggt ggtcgcgaaa 7740
ggtcctaaac tggcgaccta tggccatttt ttctggggtg atgcagtaga aggtaagcgg 7800
gtcttgttcc cagcggtccc atccaaggtt cgcggctagg tctcgcgcgg cagtcactag 7860
aggctcatct ccgccgaact tcatgaccag catgaagggc acgagctgct tcccaaaggc 7920
ccccatccaa gtataggtct ctacatcgta ggtgacaaag agacgctcgg tgcgaggatg 7980
cgagccgatc gggaagaact ggatctcccg ccaccaattg gaggagtggc tattgatgtg 8040
gtgaaagtag aagtccctgc gacgggccga acactcgtgc tggcttttgt aaaaacgtgc 8100
gcagtactgg cagcggtgca cgggctgtac atcctgcacg aggttgacct gacgaccgcg 8160
cacaaggaag cagagtggga atttgagccc ctcgcctggc gggtttggct ggtggtcttc 8220
tacttcggct gcttgtcctt gaccgtctgg ctgctcgagg ggagttacgg tggatcggac 8280
caccacgccg cgcgagccca aagtccagat gtccgcgcgc ggcggtcgga gcttgatgac 8340
aacatcgcgc agatgggagc tgtccatggt ctggagctcc cgcggcgtca ggtcaggcgg 8400

```
gagctcctgc aggtttacct cgcatagacg ggtcagggcg cgggctagat ccaggtgata   8460
cctaatttcc aggggctggt tggtggcggc gtcgatggct tgcaagaggc cgcatccccg   8520
cggcgcgact acggtaccgc gcggcgggcg gtgggccgcg gggtgtcct tggatgatgc    8580
atctaaaagc ggtgacgcgg gcgagccccc ggaggtaggg ggggctccgg acccgccggg   8640
agagggggca ggggcacgtc ggcgccgcgc gcgggcagga gctggtgctg cgcgcgtagg   8700
ttgctggcga acgcgacgac gcggcggttg atctcctgaa tctggcgcct ctgcgtgaag   8760
acgacgggcc cggtgagctt gagcctgaaa gagagttcga cagaatcaat ttcggtgtcg   8820
ttgacggcgg cctggcgcaa aatctcctgc acgtctcctg agttgtcttg ataggcgatc   8880
tcggccatga actgctcgat ctcttcctcc tggagatctc cgcgtccggc tcgctccacg   8940
gtggcggcga ggtcgttgga aatgcgggcc atgagctgcg agaaggcgtt gaggcctccc   9000
tcgttccaga cgcggctgta gaccacgccc ccttcggcat cgcgggcgcg catgaccacc   9060
tgcgcgagat tgagctccac gtgccgggcg aagacggcgt agtttcgcag gcgctgaaag   9120
aggtagttga gggtggtggc ggtgtgttct gccacgaaga agtacataac ccagcgtcgc   9180
aacgtggatt cgttgatatc ccccaaggcc tcaaggcgct ccatggcctc gtagaagtcc   9240
acggcgaagt tgaaaaactg ggagttgcgc gccgacacgg ttaactcctc ctccagaaga   9300
cggatgagct cggcgacagt gtcgcgcacc tcgcgctcaa aggctacagg ggcctcttct   9360
tcttcttcaa tctcctcttc cataagggcc tccccttctt cttcttctgg cggcggtggg   9420
ggaggggggga cacggcggcg acgacggcgc accgggaggc ggtcgacaaa gcgctcgatc   9480
atctccccgc ggcgacggcg catggtctcg gtgacggcgc ggccgttctc gcgggggcgc   9540
agttggaaga cgccgcccgt catgtcccgg ttatgggttg gcggggggct gccatgcggc   9600
agggatacgg cgctaacgat gcatctcaac aattgttgtg taggtactcc gccgccgagg   9660
gacctgagcg agtccgcatc gaccggatcg gaaaacctct cgagaaaggc gtctaaccag   9720
tcacagtcgc aaggtaggct gagcaccgtg gcgggcggca gcgggcggcg gtcggggttg   9780
tttctggcgg aggtgctgct gatgatgtaa ttaaagtagg cggtcttgag acggcggatg   9840
gtcgacagaa gcaccatgtc cttgggtccg gcctgctgaa tgcgcaggcg gtcggccatg   9900
ccccaggctt cgttttgaca tcggcgcagg tctttgtagt agtcttgcat gagcctttct   9960
accggcactt cttcttctcc ttcctcttgt cctgcatctc ttgcatctat cgctgcggcg   10020
gcggcggagt ttggccgtag gtggcgccct cttcctccca tgcgtgtgac cccgaagccc   10080
ctcatcggct gaagcagggc taggtcggcg acaacgcgct cggctaatat ggcctgctgc   10140
acctgcgtga gggtagactg gaagtcatcc atgtccacaa agcggtggta tgcgcccgtg   10200
ttgatggtgt aagtgcagtt ggccataacg gaccagttaa cggtctggtg acccggctgc   10260
gagagctcgg tgtacctgag acgcgagtaa gccctcgagt caaatacgta gtcgttgcaa   10320
gtccgcacca ggtactggta tcccaccaaa aagtgcggcg gcggctggcg gtagaggggc   10380
cagcgtaggg tggccggggc tccgggggcg agatcttcca acataaggcg atgatatccg   10440
tagatgtacc tggacatcca ggtgatgccg gcggcggtgg tggaggcgcg cggaaagtcg   10500
cggacgcggt tccagatgtt gcgcagcggc aaaaagtgct ccatggtcgg gacgctctgg   10560
ccggtcaggc gcgcgcaatc gttgacgctc tagaccgtgc aaaaggagag cctgtaagcg   10620
ggcactcttc cgtggtctgg tggataaatt cgcaagggta tcatggcgga cgaccggggt   10680
tcgagccccg tatccggccg tccgccgtga tccatgcggt taccgcccgc gtgtcgaacc   10740
caggtgtgcg acgtcagaca acgggggagt gctccttttg gcttccttcc aggcgcggcg   10800
gctgctgcgc tagctttttt ggccactggc cgcgcgcagc gtaagcggtt aggctggaaa   10860
gcgaaagcat taagtggctc gctccctgta gccggagggt tattttccaa gggttgagtc   10920
gcgggacccc cggttcgagt ctcggaccgg ccggactgcg gcgaacgggg gtttgcctcc   10980
ccgtcatgca agaccccgct tgcaaattcc tccggaaaca gggacgagcc cctttttgc    11040
ttttcccaga tgcatccggt gctgcggcag atgcgccccc ctcctcagca gcggcaagag   11100
caagagcagc ggcagacatg cagggcaccc tcccctcctc ctaccgcgtc aggaggggcg   11160
acatccgcgg ttgacgcggc agcagatggt gattacgaac cccgcggcg ccgggcccgg    11220
cactacctgg acttggagga gggcgagggc ctggcgcggc taggagcgcc ctctcctgag   11280
cggtacccaa gggtgcagct gaagcgtgat acgcgtgagg cgtacgtgcc gcggcagaac   11340
ctgtttcgcg accgcgaggg agaggagccc gaggagatgc gggatcgaaa gttccacgca   11400
gggcgcgagc tgcggcatgg cctgaatcgc gagcggttgc tgcgcgagga ggactttgag   11460
cccgacgcgc gaaccgggat tagtcccgcg cgcgcacacg tggcggccgc cgacctggta   11520
accgcatacg agcagacggt gaaccaggag attaactttc aaaaaagctt taacaaccac   11580
gtgcgtacgc ttgtggcgcg cgaggaggtg gctataggac tgatgcatct gtgggacttt   11640
gtaagcgcgc tggagcaaaa cccaaatagc aagccgctca tggcgcagct gttccttata   11700
```

gtgcagcaca gcagggacaa cgaggcattc agggatgcgc tgctaaacat agtagagccc 11760
gagggccgct ggctgctcga tttgataaac atcctgcaga gcatagtggt gcaggagcgc 11820
agcttgagcc tggctgacaa ggtggccgcc atcaactatt ccatgcttag cctgggcaag 11880
ttttacgccc gcaagatata ccataccct tacgttccca tagacaagga ggtaaagatc 11940
gaggggttct acatgcgcat ggcgctgaag gtgcttacct tgagcgacga cctgggcgtt 12000
tatcgcaacg agcgcatcca caaggccgtg agcgtgagcc ggcggcgcga gctcagcgac 12060
cgcgagctga tgcacagcct gcaaagggcc ctggctggca cgggcagcgg cgatagagag 12120
gccgagtcct actttgacgc gggcgctgac ctgcgctggg ccccaagccg acgcgccctg 12180
gaggcagctg gggccggacc tgggctggcg gtggcacccg cgcgcgctgg caacgtcggc 12240
ggcgtggagg aatatgacga ggacgatgag tacgagccag aggacggcga gtactaagcg 12300
gtgatgtttc tgatcagatg atgcaagacg caacggaccc ggcggtgcgg gcggcgctgc 12360
agagccagcc gtccggcctt aactccacgg acgactggcg ccaggtcatg gaccgcatca 12420
tgtcgctgac tgcgcgcaat cctgacgcgt tccggcagca gccgcaggcc aaccggctct 12480
ccgcaattct ggaagcggtg gtcccggcgc gcgcaaaccc cacgcacgag aaggtgctgg 12540
cgatcgtaaa cgcgctggcc gaaaacaggg ccatccggcc cgacgaggcc ggcctggtct 12600
acgacgcgct gcttcagcgc gtggctcgtt acaacagcgg caacgtgcag accaacctgg 12660
accggctggt gggggatgtg cgcgaggccg tggcgcagcg tgagcgcgcg cagcagcagg 12720
gcaacctggg ctccatggtt gcactaaacg ccttcctgag tacacagccc gccaacgtgc 12780
cgcggggaca ggaggactac accaactttg tgagcgcact gcggctaatg gtgactgaga 12840
caccgcaaag tgaggtgtac cagtctgggc cagactattt tttccagacc agtagacaag 12900
gcctgcagac cgtaaacctg agccaggctt tcaaaaactt gcaggggctg tggggggtgc 12960
gggctcccac aggcgaccgc gcgaccgtgt ctagcttgct gacgcccaac tcgcgcctgt 13020
tgctgctgct aatagcgccc ttcacggaca gtggcagcgt gtcccgggac acatacctag 13080
gtcacttgct gacactgtac cgcgaggcca taggtcaggc gcatgtggac gagcatactt 13140
tccaggagat tacaagtgtc agccgcgcgc tggggcagga ggacacgggc agcctggagg 13200
caaccctaaa ctacctgctg accaaccggc ggcagaagat cccctcgttg cacagtttaa 13260
acagcgagga ggagcgcatt ttgcgctacg tgcagcagag cgtgagcctt aacctgatgc 13320
gcgacggggt aacgcccagc gtggcgctgg acatgaccgc gcgcaacatg gaaccgggca 13380
tgtatgcctc aaaccggccg tttatcaacc gcctaatgga ctacttgcat cgcgcggccg 13440
ccgtgaaccc cgagtatttc accaatgcca tcttgaaccc gcactggcta ccgccccctg 13500
gtttctacac cgggggattc gaggtgcccg agggtaacga tggattcctc tgggacgaca 13560
tagacgacag cgtgttttcc ccgcaaccgc agaccctgct agagttgcaa cagcgcgagc 13620
aggcagaggc ggcgctgcga aaggaaagct tccgcaggcc aagcagcttg tccgatctag 13680
gcgctgcggc cccgcggtca gatgctagta gcccatttcc aagcttgata gggtctctta 13740
ccagcactcg caccacccgc ccgcgcctgc tgggcgagga ggagtaccta aacaactcgc 13800
tgctgcagcc gcagcgcgaa aaaaacctgc ctccggcatt tcccaacaac gggatagaga 13860
gcctagtgga caagatgagt agatggaaga cgtacgcgca ggagcacagg gacgtgccag 13920
gcccgcgccc gcccacccgt cgtcaaaggc acgaccgtca gcggggtctg gtgtgggagg 13980
acgatgactc ggcagacgac agcagcgtcc tggatttggg agggagtggc aacccgtttg 14040
cgcaccttcg ccccaggctg gggagaatgt tttaaaaaaa aaaaagcatg atgcaaaata 14100
aaaaactcac caaggccatg gcaccgagcg ttggttttct tgtattcccc ttagtatgcg 14160
gcgcgcggcg atgtatgagg aaggtcctcc tccctcctac gagagtgtgg tgagcgcggc 14220
gccagtggcg gcggcgctgg gttctccctt cgatgctccc ctggacccgc cgtttgtgcc 14280
tccgcggtac ctgcggccta ccggggggag aaacagcatc cgttactctg agttggcacc 14340
cctattcgac accacccgtg tgtacctggt ggacaacaag tcaacggatg tggcatccct 14400
gaactaccag aacgaccaca gcaactttct gaccacggtc attcaaaaca atgactacag 14460
cccgggggag gcaagcacac agaccatcaa tcttgacgac cggtcgcact ggggcggcga 14520
cctgaaaacc atcctgcata ccaacatgcc aaatgtgaac gagttcatgt ttaccaataa 14580
gtttaaggcg cgggtgatgg tgtcgcgctt gcctactaag gacaatcagg tggagctgaa 14640
atacgagtgg gtggagttca cgctgcccga gggcaactac tccgagacca tgaccataga 14700
ccttatgaac aacgcgatcg tggagcacta cttgaaagtg ggcagacaga acggggttct 14760
ggaaagcgac atcggggtaa agtttgacac ccgcaacttc agactggggt ttgaccccgt 14820
cactggtctt gtcatgcctg gggtatatac aaacgaagcc ttccatccag acatcatttt 14880
gctgccagga tgcggggtgg acttcaccca cagccgcctg agcaacttgt tgggcatccg 14940
caagcggcaa cccttccagg agggctttag gatcacctac gatgatctgg agggtggtaa 15000

cattcccgca ctgttggatg tggacgccta ccaggcgagc ttgaaagatg acaccgaaca 15060
gggcgggggt ggcgcaggcg gcagcaacag cagtggcagc ggcgcggaag agaactccaa 15120
cgcggcagcc gcggcaatgc agccggtgga ggacatgaac gatcatgcca ttcgcggcga 15180
cacctttgcc acacgggctg aggagaagcg cgctgaggcc gaagcagcgg ccgaagctgc 15240
cgcccccgct gcgcaacccg aggtcgagaa gcctcagaag aaaccggtga tcaaacccct 15300
gacagaggac agcaagaaac gcagttacaa cctaataagc aatgacagca ccttcaccca 15360
gtaccgcagc tggtaccttg catacaacta cggcgaccct cagaccggaa tccgctcatg 15420
gaccctgctt tgcactcctg acgtaacctg cggctcggag caggtctact ggtcgttgcc 15480
agacatgatg caagaccccg tgaccttccg ctccacgcgc cagatcagca actttccggt 15540
ggtgggcgcc gagctgttgc ccgtgcactc caagagcttc tacaacgacc aggccgtcta 15600
ctcccaactc atccgccagt ttacctctct gacccacgtg ttcaatcgct ttcccgagaa 15660
ccagattttg gcgcgcccgc cagcccccac catcaccacc gtcagtgaaa acgttcctgc 15720
tctcacagat cacgggacgc taccgctgcg caacagcatc ggaggagtcc agcgagtgac 15780
cattactgac gccagacgcc gcacctgccc ctacgtttac aaggccctgg gcatagtctc 15840
gccgcgcgtc ctatcgagcc gcactttttg agcaagcatg tccatcctta tatcgcccag 15900
caataacaca ggctggggcc tgcgcttccc aagcaagatg tttggcgggg ccaagaagcg 15960
ctccgaccaa cacccagtgc gcgtgcgcgg gcactaccgc gcgccctggg gcgcgcacaa 16020
acgcggccgc actgggcgca ccaccgtcga tgacgccatc gacgcggtgg tggaggaggc 16080
gcgcaactac acgcccacgc cgccaccagt gtccacagtg gacgcggcca ttcagaccgt 16140
ggtgcgcgga gcccggcgct atgctaaaat gaagagacgg cggaggcgcg tagcacgtcg 16200
ccaccgccgc cgacccggca ctgccgccca acgcgcggcg gcggccctgc ttaaccgcgc 16260
acgtcgcacc ggccgacggg cggccatgcg ggccgctcga aggctggccg cgggtattgt 16320
cactgtgccc cccaggtcca ggcgacgagc ggccgccgca gcagccgcgg ccattagtgc 16380
tatgactcag ggtcgcaggg gcaacgtgta ttgggtgcgc gactcggtta gcggcctgcg 16440
cgtgcccgtg cgcacccgcc ccccgcgcaa ctagattgca agaaaaaact acttagactc 16500
gtactgttgt atgtatccag cggcggcggc gcgcaacgaa gctatgtcca agcgcaaaat 16560
caaagaagag atgctccagg tcatcgcgcc ggagatctat ggccccccga agaaggaaga 16620
gcaggattac aagccccgaa agctaaagcg ggtcaaaaag aaaaagaaag atgatgatga 16680
tgaacttgac gacgaggtgg aactgctgca cgctaccgcg cccaggcgac gggtacagtg 16740
gaaaggtcga cgcgtaaaac gtgttttgcg acccggcacc accgtagtct ttacgcccgg 16800
tgagcgctcc acccgcacct acaagcgcgt gtatgatgag gtgtacggcg acgaggacct 16860
gcttgagcag gccaacgagc gcctcgggga gtttgcctac ggaaagcggc ataaggacat 16920
gctggcgttg ccgctggacg agggcaaccc aacacctagc ctaaagcccg taacactgca 16980
gcaggtgctg cccgcgcttg caccgtccga agaaaagcgc ggcctaaagc gcgagtctgg 17040
tgacttggca cccaccgtgc agctgatggt acccaagcgc cagcgactgg aagatgtctt 17100
ggaaaaaatg accgtggaac ctgggctgga gcccgaggtc cgcgtgcggc caatcaagca 17160
ggtggcgccg ggactgggcg tgcagaccgt ggacgttcag atacccacta ccagtagcac 17220
cagtattgcc accgccacag agggcatgga gacacaaacg tccccggttg cctcagcggt 17280
ggcggatgcc gcggtgcagg cggtcgctgc ggccgcgtcc aagacctcta cggaggtgca 17340
aacggacccg tggatgtttc gcgtttcagc cccccggcgc ccgcgcggtt cgaggaagta 17400
cggcgccgcc agcgcgctac tgcccgaata tgccctacat ccttccattg cgcctacccc 17460
cggctatcgt ggctacacct accgccccag aagacgagca actacccgac gccgaaccac 17520
cactggaacc cgccgccgcc gtcgccgtcg ccagcccgtg ctggccccga tttccgtgcg 17580
cagggtggct cgcgaaggag gcaggaccct ggtgctgcca acagcgcgct accaccccag 17640
catcgtttaa aagccggtct ttgtggttct tgcagatatg gccctcacct gccgcctccg 17700
tttcccggtg ccgggattcc gaggaagaat gcaccgtagg aggggcatgg ccggccacgg 17760
cctgacgggc ggcatgcgtc gtgcgcacca ccggcggcgg cgcgcgtcgc accgtcgcat 17820
gcgcggcggt atcctgcccc tccttattcc actgatcgcc gcggcgattg gcgccgtgcc 17880
cggaattgca tccgtggcct tgcaggcgca gagacactga ttaaaaacaa gttgcatgtg 17940
gaaaaatcaa aataaaaagt ctggactctc acgctcgctt ggtcctgtaa ctattttgta 18000
gaatggaaga catcaacttt gcgtctctgg ccccgcgaca cggctcgcgc ccgttcatgg 18060
gaaactggca agatatcggc accagcaata tgagcggtgg cgccttcagc tggggctcgc 18120
tgtggagcgg cattaaaaat ttcggttcca ccgttaagaa ctatggcagc aaggcctgga 18180
acagcagcac aggccagatg ctgagggata agttgaaaga gcaaaatttc caacaaaagg 18240
tggtagatgg cctggcctct ggcattagcg gggtggtgga cctggccaac caggcagtgc 18300

aaaataagat taacagtaag cttgatcccc gccctcccgt agaggagcct ccaccggccg 18360
tggagacagt gtctccagag gggcgtggcg aaaagcgtcc gcgccccgac agggaagaaa 18420
ctctggtgac gcaaatagac gagcctccct cgtacgagga ggcactaaag caaggcctgc 18480
ccaccacccg tcccatcgcg cccatggcta ccggagtgct gggccagcac acacccgtaa 18540
cgctggacct gcctcccccc gccgacaccc agcagaaacc tgtgctgcca ggcccgaccg 18600
ccgttgttgt aacccgtcct agccgcgcgt ccctgcgccg cgccgccagc ggtccgcgat 18660
cgttgcggcc cgtagccagt ggcaactggc aaagcacact gaacagcatc gtgggtctgg 18720
gggtgcaatc cctgaagcgc cgacgatgct tctgaatagc taacgtgtcg tatgtgtgtc 18780
atgtatgcgt ccatgtcgcc gccagaggag ctgctgagcc gccgcgcgcc cgctttccaa 18840
gatggctacc ccttcgatga tgccgcagtg gtcttacatg cacatctcgg gccaggacgc 18900
ctcggagtac ctgagccccg ggctggtgca gtttgcccgc gccaccgaga cgtacttcag 18960
cctgaataac aagtttagaa accccacggt ggcgcctacg cacgacgtga ccacagaccg 19020
gtcccagcgt ttgacgctgc ggttcatccc tgtggaccgt gaggatactg cgtactcgta 19080
caaggcgcgg ttcaccctag ctgtgggtga taaccgtgtg ctggacatgg cttccacgta 19140
ctttgacatc cgcggcgtgc tggacagggg ccctactttt aagccctact ctggcactgc 19200
ctacaacgcc ctggctccca agggtgcccc aaatccttgc gaatgggatg aagctgctac 19260
tgctcttgaa ataaacctag aagaagagga cgatgacaac gaagacgaag tagacgagca 19320
agctgagcag caaaaaactc acgtatttgg gcaggcgcct tattctggta taaatattac 19380
aaaggagggt attcaaatag gtgtcgaagg tcaaacacct aaatatgccg ataaaacatt 19440
tcaacctgaa cctcaaatag gagaatctca gtggtacgaa actgaaatta atcatgcagc 19500
tgggagagtc cttaaaaaga ctaccccaat gaaaccatgt tacggttcat atgcaaaacc 19560
cacaaatgaa aatggagggc aaggcattct tgtaaagcaa caaaatggaa agctagaaag 19620
tcaagtggaa atgcaatttt tctcaactac tgaggcgacc gcaggcaatg gtgataactt 19680
gactcctaaa gtggtattgt acagtgaaga tgtagatata gaaaccccag acactcatat 19740
ttcttacatg cccactatta aggaaggtaa ctcacgagaa ctaatgggcc aacaatctat 19800
gcccaacagg cctaattaca ttgcttttag ggacaatttt attggtctaa tgtattacaa 19860
cagcacgggt aatatgggtg ttctggcggg ccaagcatcg cagttgaatg ctgttgtaga 19920
tttgcaagac agaaacacag agctttcata ccagcttttg cttgattcca ttggtgatag 19980
aaccaggtac ttttctatgt ggaatcaggc tgttgacagc tatgatccag atgttagaat 20040
tattgaaaat catggaactg aagatgaact tccaaattac tgctttccac tgggaggtgt 20100
gattaataca gagactctta ccaaggtaaa acctaaaaca ggtcaggaaa atggatggga 20160
aaaagatgct acagaatttt cagataaaaa tgaaataaga gttggaaata attttgccat 20220
ggaaatcaat ctaaatgcca acctgtggag aaatttcctg tactccaaca tagcgctgta 20280
tttgcccgac aagctaaagt acagtccttc caacgtaaaa atttctgata acccaaacac 20340
ctacgactac atgaacaagc gagtggtggc tcccgggtta gtggactgct acattaacct 20400
tggagcacgc tggtcccttg actatatgga caacgtcaac ccatttaacc accaccgcaa 20460
tgctggcctg cgctaccgct caatgttgct gggcaatggt cgctatgtgc ccttccacat 20520
ccaggtgcct cagaagttct ttgccattaa aaacctcctt ctcctgccgg gctcatacac 20580
ctacgagtgg aacttcagga aggatgttaa catggttctg cagagctccc taggaaatga 20640
cctaagggtt gacggagcca gcattaagtt tgatagcatt tgcctttacg ccaccttctt 20700
ccccatggcc cacaacaccg cctccacgct tgaggccatg cttagaaacg acaccaacga 20760
ccagtccttt aacgactatc tctccgccgc caacatgctc taccctatac ccgccaacgc 20820
taccaacgtg cccatatcca tcccctcccg caactgggcg gctttccgcg gctgggcctt 20880
cacgcgcctt aagactaagg aaaccccatc actgggctcg ggctacgacc cttattacac 20940
ctactctggc tctataccct acctagatgg aacctttac ctcaaccaca cctttaagaa 21000
ggtggccatt acctttgact cttctgtcag ctggcctggc aatgaccgcc tgcttacccc 21060
caacgagttt gaaattaagc gctcagttga cggggagggt tacaacgttg cccagtgtaa 21120
catgaccaaa gactggttcc tggtacaaat gctagctaac tacaacattg gctaccaggg 21180
cttctatatc ccagagagct acaaggaccg catgtactcc ttctttagaa acttccagcc 21240
catgagccgt caggtggtgg atgatactaa atacaaggac taccaacagg tgggcatcct 21300
acaccaacac aacaactctg gatttgttgg ctaccttgcc cccaccatgc gcgaaggaca 21360
ggcctaccct gctaacttcc cctatccgct tataggcaag accgcagttg acagcattac 21420
ccagaaaaag tttctttgcg atcgcaccct ttggcgcatc ccattctcca gtaactttat 21480
gtccatgggc gcactcacag acctgggcca aaaccttctc tacgccaact ccgcccacgc 21540
gctagacatg acttttgagg tggatcccat ggacgagccc acccttcttt atgttttgtt 21600

tgaagtcttt gacgtggtcc gtgtgcaccg gccgcaccgc ggcgtcatcg aaaccgtgta 21660
cctgcgcacg cccttctcgg ccggcaacgc cacaacataa agaagcaagc aacatcaaca 21720
acagctgccg ccatgggctc cagtgagcag gaactgaaag ccattgtcaa agatcttggt 21780
tgtgggccat atttttggg cacctatgac aagcgctttc caggctttgt ttctccacac 21840
aagctcgcct gcgccatagt caatacggcc ggtcgcgaga ctgggggcgt acactggatg 21900
gcctttgcct ggaacccgca ctcaaaaaca tgctacctct ttgagccctt tggcttttct 21960
gaccagcgac tcaagcaggt ttaccagttt gagtacgagt cactcctgcg ccgtagcgcc 22020
attgcttctt cccccgaccg ctgtataacg ctggaaaagt ccacccaaag cgtacagggg 22080
cccaactcgg ccgcctgtgg actattctgc tgcatgtttc tccacgcctt tgccaactgg 22140
ccccaaactc ccatggatca caaccccacc atgaacctta ttaccggggt acccaactcc 22200
atgctcaaca gtccccaggt acagcccacc ctgcgtcgca accaggaaca gctctacagc 22260
ttcctggagc gccactcgcc ctacttccgc agccacagtg cgcagattag gagcgccact 22320
tctttttgtc acttgaaaaa catgtaaaaa taatgtacta gagacacttt caataaaggc 22380
aaatgctttt atttgtacac tctcgggtga ttatttaccc ccacccttgc cgtctgcgcc 22440
gtttaaaaat caaaggggtt ctgccgcgca tcgctatgcg ccactggcag ggacacgttg 22500
cgatactggt gtttagtgct ccacttaaac tcaggcacaa ccatccgcgg cagctcggtg 22560
aagttttcac tccacaggct gcgcaccatc accaacgcgt ttagcaggtc gggcgccgat 22620
atcttgaagt cgcagttggg gcctccgccc tgcgcgcgcg agttgcgata cacagggttg 22680
cagcactgga acactatcag cgccgggtgg tgcacgctgg ccagcacgct cttgtcggag 22740
atcagatccg cgtccaggtc ctccgcgttg ctcagggcga acggagtcaa ctttggtagc 22800
tgccttccca aaaagggcgc gtgcccaggc tttgagttgc actcgcaccg tagtggcatc 22860
aaaaggtgac cgtgcccggt ctgggcgtta ggatacagcg cctgcataaa agccttgatc 22920
tgcttaaaag ccacctgagc ctttgcgcct tcagagaaga acatgccgca agacttgccg 22980
gaaaactgat tggccggaca ggccgcgtcg tgcacgcagc accttgcgtc ggtgttggag 23040
atctgcacca catttcggcc ccaccggttc ttcacgatct tggccttgct agactgctcc 23100
ttcagcgcgc gctgcccgtt ttcgctcgtc acatccattt caatcacgtg ctccttattt 23160
atcataatgc ttccgtgtag acacttaagc tcgccttcga tctcagcgca gcggtgcagc 23220
cacaacgcgc agcccgtggg ctcgtgatgc ttgtaggtca cctctgcaaa cgactgcagg 23280
tacgcctgca ggaatcgccc catcatcgtc acaaaggtct tgttgctggt gaaggtcagc 23340
tgcaacccgc ggtgctcctc gttcagccag gtcttgcata cggccgccag agcttccact 23400
tggtcaggca gtagtttgaa gttcgccttt agatcgttat ccacgtggta cttgtccatc 23460
agcgcgcgcg cagcctccat gcccttctcc cacgcagaca cgatcggcac actcagcggg 23520
ttcatcaccg taatttcact ttccgcttcg ctgggctctt cctcttcctc ttgcgtccgc 23580
ataccacgcg ccactgggtc gtcttcattc agccgccgca ctgtgcgctt acctcctttg 23640
ccatgcttga ttagcaccgg tgggttgctg aaacccacca tttgtagcgc cacatcttct 23700
ctttcttcct cgctgtccac gattacctct ggtgatggcg ggcgctcggg cttgggagaa 23760
gggcgcttct ttttcttctt gggcgcaatg gccaaatccg ccgccgaggt cgatggccgc 23820
gggctgggtg tgcgcggcac cagcgcgtct tgtgatgagt cttcctcgtc ctcggactcg 23880
atacgccgcc tcatccgctt ttttgggggc gcccggggag gcggcggcga cggggacggg 23940
gacgacacgt cctccatggt tgggggacgt cgcgccgcac cgcgtccgcg ctcgggggtg 24000
gtttcgcgct gctcctcttc ccgactggcc atttccttct cctataggca gaaaaagatc 24060
atggagtcag tcgagaagaa ggacagccta accgcccccct ctgagttcgc caccaccgcc 24120
tccaccgatg ccgccaacgc gcctaccacc ttccccgtcg aggcaccccc gcttgaggag 24180
gaggaagtga ttatcgagca ggacccaggt tttgtaagcg aagacgacga ggaccgctca 24240
gtaccaacag aggataaaaa gcaagaccag gacaacgcag aggcaaacga ggaacaagtc 24300
gggcgggggg acgaaaggca tggcgactac ctagatgtgg gagacgacgt gctgttgaag 24360
catctgcagc gccagtgcgc cattatctgc gacgcgttgc aagagcgcag cgatgtgccc 24420
ctcgccatag cggatgtcag ccttgcctac gaacgccacc tattctcacc gcgcgtaccc 24480
cccaaacgcc aagaaaacgg cacatgcgag cccaacccgc gcctcaactt ctaccccgta 24540
tttgccgtgc cagaggtgct tgccacctat cacatctttt tccaaaactg caagataccc 24600
ctatcctgcc gtgccaaccg cagccgagcg gacaagcagc tggccttgcg gcagggcgct 24660
gtcatacctg atatcgcctc gctcaacgaa gtgccaaaaa tctttgaggg tcttggacgc 24720
gacgagaagc gcgcggcaaa cgctctgcaa caggaaaaca gcgaaaatga aagtcactct 24780
ggagtgttgg tggaactcga gggtgacaac gcgcgcctag ccgtactaaa acgcagcatc 24840
gaggtcaccc actttgccta cccggcactt aacctacccc ccaaggtcat gagcacagtc 24900

atgagtgagc tgatcgtgcg ccgtgcgcag cccctggaga gggatgcaaa tttgcaagaa 24960
caaacagagg agggcctacc cgcagttggc gacgagcagc tagcgcgctg gcttcaaacg 25020
cgcgagcctg ccgacttgga ggagcgacgc aaactaatga tggccgcagt gctcgttacc 25080
gtggagcttg agtgcatgca gcggttcttt gctgacccgg agatgcagcg caagctagag 25140
gaaacattgc actacacctt tcgacagggc tacgtacgcc aggcctgcaa gatctccaac 25200
gtggagctct gcaacctggt ctcctacctt ggaattttgc acgaaaaccg ccttgggcaa 25260
aacgtgcttc attccacgct caagggcgag gcgcgccgcg actacgtccg cgactgcgtt 25320
tacttatttc tatgctacac ctggcagacg gccatgggcg tttggcagca gtgcttggag 25380
gagtgcaacc tcaaggagct gcagaaactg ctaaagcaaa acttgaagga cctatggacg 25440
gccttcaacg agcgctccgt ggccgcgcac ctggcggaca tcattttccc cgaacgcctg 25500
cttaaaaccc tgcaacaggg tctgccagac ttcaccagtc aaagcatgtt gcagaacttt 25560
aggaacttta tcctagagcg ctcaggaatc ttgcccgcca cctgctgtgc acttcctagc 25620
gactttgtgc ccattaagta ccgcgaatgc cctccgccgc tttggggcca ctgctacctt 25680
ctgcagctag ccaactacct tgcctaccac tctgacataa tggaagacgt gagcggtgac 25740
ggtctactgg agtgtcactg tcgctgcaac ctatgcaccc cgcaccgctc cctggtttgc 25800
aattcgcagc tgcttaacga aagtcaaatt atcggtacct ttgagctgca gggtccctcg 25860
cctgacgaaa agtccgcggc tccggggttg aaactcactc cggggctgtg gacgtcggct 25920
taccttcgca aatttgtacc tgaggactac cacgcccacg agattaggtt ctacgaagac 25980
caatcccgcc cgccaaatgc ggagcttacc gcctgcgtca ttacccaggg ccacattctt 26040
ggccaattgc aagccatcaa caaagcccgc caagagtttc tgctacgaaa gggacggggg 26100
gtttacttgg acccccagtc cggcgaggag ctcaacccaa tcccccgcc gccgcagccc 26160
tatcagcagc agccgcgggc ccttgcttcc caggatggca cccaaaaaga agctgcagct 26220
gccgccgcca cccacggacg aggaggaata ctgggacagt caggcagagg aggttttgga 26280
cgaggaggag gaggacatga tggaagactg ggagagccta gacgaggaag cttccgaggt 26340
cgaagaggtg tcagacgaaa caccgtcacc ctcggtcgca ttcccctcgc cggcgcccca 26400
gaaatcggca accggttcca gcatggctac aacctccgct cctcaggcgc cgccggcact 26460
gcccgttcgc cgacccaacc gtagatggga caccactgga accagggccg gtaagtccaa 26520
gcagccgccg ccgttagccc aagagcaaca acagcgccaa ggctaccgct catggcgcgg 26580
gcacaagaac gccatagttg cttgcttgca agactgtggg ggcaacatct ccttcgcccg 26640
ccgctttctt ctctaccatc acggcgtggc cttcccccgt aacatcctgc attactaccg 26700
tcatctctac agcccatact gcaccggcgg cagcggcagc ggcagcaaca gcagcggcca 26760
cacagaagca aaggcgaccg gatagcaaga ctctgacaaa gcccaagaaa tccacagcgg 26820
cggcagcagc aggaggagga gcgctgcgtc tggcgcccaa cgaacccgta tcgacccgcg 26880
agcttagaaa caggattttt cccactctgt atgctatatt tcaacagagc aggggccaag 26940
aacaagagct gaaaataaaa aacaggtctc tgcgatccct cacccgcagc tgcctgtatc 27000
acaaaagcga agatcagctt cggcgcacgc tggaagacgc ggaggctctc ttcagtaaat 27060
actgcgcgct gactcttaag gactagtttc gcgccctttc tcaaatttaa gcgcgaaaac 27120
tacgtcatct ccagcggcca cacccggcgc cagcacctgt cgtcagcgcc attatgagca 27180
aggaaattcc cacgccctac atgtggagtt accagccaca aatgggactt gcggctggag 27240
ctgcccaaga ctactcaacc cgaataaact acatgagcgc gggaccccac atgatatccc 27300
gggtcaacgg aatccgcgcc caccgaaacc gaattctctt ggaacaggcg gctattacca 27360
ccacacctcg taataacctt aatccccgta gttggcccgc tgccctggtg taccaggaaa 27420
gtcccgctcc caccactgtg gtacttccca gagacgccca ggccgaagtt cagatgacta 27480
actcaggggc gcagcttgcg ggcggctttc gtcacagggt gcggtcgccc gggcagggta 27540
taactcacct gacaatcaga gggcgaggta ttcagctcaa cgacgagtcg gtgagctcct 27600
cgcttggtct ccgtccggac gggacatttc agatcggcgg cgccggccgt ccttcattca 27660
cgcctcgtca ggcaatccta actctgcaga cctcgtcctc tgagccgcgc tctggaggca 27720
ttggaactct gcaatttatt gaggagtttg tgccatcggt ctactttaac cccttctcgg 27780
gacctcccgg ccactatccg gatcaattta ttcctaactt tgacgcggta aaggactcgg 27840
cggacggcta cgactgaatg ttaagtggag aggcagagca actgcgcctg aaacacctgg 27900
tccactgtcg ccgccacaag tgctttgccc gcgactccgg tgagttttgc tactttgaat 27960
tgcccgagga tcatatcgag ggcccggcgc acggcgtccg gcttaccgcc cagggagagc 28020
ttgcccgtag cctgattcgg gagtttaccc agcgccccct gctagttgag cgggacaggg 28080
gaccctgtgt tctcactgtg atttgcaact gtcctaacct tggattacat caagatcttt 28140
gttgccatct ctgtgctgag tataataaat acagaaatta aaatatactg gggctcctat 28200

cgccatcctg taaacgccac cgtcttcacc cgcccaagca aaccaaggcg aaccttacct 28260
ggtactttta acatctctcc ctctgtgatt tacaacagtt tcaacccaga cggagtgagt 28320
ctacgagaga acctctccga gctcagctac tccatcagaa aaaacaccac cctccttacc 28380
tgccgggaac gtacgagtgc gtcaccggcc gctgcaccac acctaccgcc tgaccgtaaa 28440
ccagactttt tccggacaga cctcaataac tctgtttacc agaacaggag gtgagcttag 28500
aaaaccctta gggtattagg ccaaaggcgc agctactgtg gggtttatga acaattcaag 28560
caactctacg ggctattcta attcaggttt ctctagaatc ggggttgggg ttattctctg 28620
tcttgtgatt ctctttattc ttatactaac gcttctctgc ctaaggctcg ccgcctgctg 28680
tgtgcacatt tgcatttatt gtcagctttt taaacgctgg ggtcgccacc caagatgatt 28740
aggtacataa tcctaggttt actcaccctt gcgtcagccc acggtaccac ccaaaaggtg 28800
gattttaagg agccagcctg taatgttaca ttcgcagctg aagctaatga gtgcaccact 28860
cttataaaat gcaccacaga acatgaaaag ctgcttattc gccacaaaaa caaaattggc 28920
aagtatgctg tttatgctat ttggcagcca ggtgacacta cagagtataa tgttacagtt 28980
ttccagggta aaagtcataa aacttttatg tatactttc cattttatga aatgtgcgac 29040
attaccatgt acatgagcaa acagtataag ttgtggcccc cacaaaattg tgtggaaaac 29100
actggcactt tctgctgcac tgctatgcta attacagtgc tcgctttggt ctgtacccta 29160
ctctatatta aatacaaaag cagacgcagc tttattgagg aaaagaaaat gccttaattt 29220
actaagttac aaagctaatg tcaccactaa ctgctttact cgctgcttgc aaaacaaatt 29280
caaaaagtta gcattataat tagaatagga tttaaacccc ccggtcattt cctgctcaat 29340
accattcccc tgaacaattg actctatgtg ggatatgctc cagcgctaca accttgaagt 29400
caggcttcct ggatgtcagc atctgacttt ggccagcacc tgtcccgcgg atttgttcca 29460
gtccaactac agcgacccac cctaacagag atgaccaaca caaccaacgc ggccgccgct 29520
accggactta catctaccac aaatacaccc caagtttctg cctttgtcaa taactgggat 29580
aacttgggca tgtggtggtt ctccatagcg cttatgtttg tatgccttat tattatgtgg 29640
ctcatctgct gcctaaagcg caaacgcgcc cgaccaccca tctatagtcc catcattgtg 29700
ctacacccaa acaatgatgg aatccataga ttggacggac tgaaacacat gttcttttct 29760
cttacagtat gattaaatga gacatgattc ctcgagtttt tatattactg acccttgttg 29820
cgcttttttg tgcgtgctcc acattggctg cggtttctca catcgaagta gactgcattc 29880
cagccttcac agtctatttg ctttacggat ttgtcaccct cacgctcatc tgcagcctca 29940
tcactgtggt catcgccttt atccagtgca ttgactgggt ctgtgtgcgc tttgcatatc 30000
tcagacacca tccccagtac agggacagga ctatagctga gcttcttaga attctttaat 30060
tatgaaattt actgtgactt ttctgctgat tatttgcacc ctatctgcgt tttgttcccc 30120
gacctccaag cctcaaagac atatatcatg cagattcact cgtatatgga atattccaag 30180
ttgctacaat gaaaaaagcg atctttccga agcctggtta tatgcaatca tctctgttat 30240
ggtgttctgc agtaccatct tagccctagc tatatatccc taccttgaca ttggctggaa 30300
acgaatagat gccatgaacc acccaacttt ccccgcgccc gctatgcttc cactgcaaca 30360
agttgttgcc ggcggctttg tcccagccaa tcagcctcgc cccacttctc ccaccccccac 30420
tgaaatcagc tactttaatc taacaggagg agatgactga caccctagat ctagaaatgg 30480
acggaattat tacagagcag cgcctgctag aaagacgcag ggcagcggcc gagcaacagc 30540
gcatgaatca agagctccaa gacatggtta acttgcacca gtgcaaaagg ggtatctttt 30600
gtctggtaaa gcaggccaaa gtcacctacg acagtaatac caccggacac cgccttagct 30660
acaagttgcc aaccaagcgt cagaaattgg tggtcatggt gggagaaaag cccattacca 30720
taactcagca ctcggtagaa accgaaggct gcattcactc accttgtcaa ggacctgagg 30780
atctctgcac ccttattaag accctgtgcg gtctcaaaga tcttattccc tttaactaat 30840
aaaaaaaaat aataaagcat cacttactta aaatcagtta gcaaatttct gtccagttta 30900
ttcagcagca cctccttgcc ctcctcccag ctctggtatt gcagcttcct cctggctgca 30960
aactttctcc acaatctaaa tggaatgtca gtttcctcct gttcctgtcc atccgcaccc 31020
actatcttca tgttgttgca gatgaagcgc gcaagaccgt ctgaagatac cttcaacccc 31080
gtgtatccat atgacacgga aaccggtcct ccaactgtgc cttttcttac tcctcccttt 31140
gtatccccca atgggtttca agagagtccc cctggggtac tctctttgcg cctatccgaa 31200
cctctagtta cctccaatgg catgcttgcg ctcaaaatgg gcaacggcct ctctctggac 31260
gaggccggca accttacctc ccaaaatgta accactgtga gcccacctct caaaaaaacc 31320
aagtcaaaca taaacctgga aatatctgca cccctcacag ttacctcaga agccctaact 31380
gtggctgccg ccgcacctct aatggtcgcg ggcaacacac tcaccatgca atcacaggcc 31440
ccgctaaccg tgcacgactc caaacttagc attgccaccc aaggacccct cacagtgtca 31500

gaaggaaagc tagccctgca aacatcaggc cccctcacca ccaccgatag cagtaccctt 31560
actatcactg cctcaccccc tctaactact gccactggta gcttgggcat tgacttgaaa 31620
gagcccattt atacacaaaa tggaaaacta ggactaaagt acggggctcc tttgcatgta 31680
acagacgacc taaacacttt gaccgtagca actggtccag gtgtgactat taataatact 31740
tccttgcaaa ctaaagttac tggagccttg ggttttgatt cacaaggcaa tatgcaactt 31800
aatgtagcag gaggactaag gattgattct caaaacagac gccttatact tgatgttagt 31860
tatccgtttg atgctcaaaa ccaactaaat ctaagactag gacagggccc tctttttata 31920
aactcagccc acaacttgga tattaactac aacaaaggcc tttacttgtt tacagcttca 31980
aacaattcca aaaagcttga ggttaaccta agcactgcca aggggttgat gtttgacgct 32040
acagccatag ccattaatgc aggagatggg cttgaatttg gttcacctaa tgcaccaaac 32100
acaaatcccc tcaaaacaaa aattggccat ggcctagaat ttgattcaaa caaggctatg 32160
gttcctaaac taggaactgg ccttagtttt gacagcacag gtgccattac agtaggaaac 32220
aaaaataatg ataagctaac tttgtggacc acaccagctc catctcctaa ctgtagacta 32280
aatgcagaga aagatgctaa actcactttg gtcttaacaa aatgtggcag tcaaatactt 32340
gctacagttt cagttttggc tgttaaaggc agtttggctc caatatctgg aacagttcaa 32400
agtgctcatc ttattataag atttgacgaa aatggagtgc tactaaacaa ttccttcctg 32460
gacccagaat attggaactt tagaaatgga gatcttactg aaggcacagc ctatacaaac 32520
gctgttggat ttatgcctaa cctatcagct tatccaaaat ctcacggtaa aactgccaaa 32580
agtaacattg tcagtcaagt ttacttaaac ggagacaaaa ctaaacctgt aacactaacc 32640
attacactaa acggtacaca ggaaacagga gacacaactc caagtgcata ctctatgtca 32700
ttttcatggg actggtctgg ccacaactac attaatgaaa tatttgccac atcctcttac 32760
actttttcat acattgccca agaataaaga atcgtttgtg ttatgtttca acgtgtttat 32820
ttttcaattg cagaaaattt caagtcattt ttcattcagt agtatagccc caccaccaca 32880
tagcttatac agatcaccgt accttaatca aactcacaga accctagtat tcaacctgcc 32940
acctccctcc caacacacag agtacacagt cctttctccc cggctggcct taaaaagcat 33000
catatcatgg gtaacagaca tattcttagg tgttatattc cacacggttt cctgtcgagc 33060
caaacgctca tcagtgatat taataaactc cccgggcagc tcacttaagt tcatgtcgct 33120
gtccagctgc tgagccacag gctgctgtcc aacttgcggt tgcttaacgg gcggcgaagg 33180
agaagtccac gcctacatgg gggtagagtc ataatcgtgc atcaggatag ggcggtggtg 33240
ctgcagcagc gcgcgaataa actgctgccg ccgccgctcc gtcctgcagg aatacaacat 33300
ggcagtggtc tcctcagcga tgattcgcac cgcccgcagc ataaggcgcc ttgtcctccg 33360
ggcacagcag cgcaccctga tctcacttaa atcagcacag taactgcagc acagcaccac 33420
aatattgttc aaaatcccac agtgcaaggc gctgtatcca aagctcatgg cggggaccac 33480
agaacccacg tggccatcat accacaagcg caggtagatt aagtggcgac ccctcataaa 33540
cacgctggac ataaacatta cctcttttgg catgttgtaa ttcaccacct cccggtacca 33600
tataaacctc tgattaaaca tggcgccatc caccaccatc ctaaaccagc tggccaaaac 33660
ctgcccgccg gctatacact gcagggaacc gggactggaa caatgacagt ggagagccca 33720
ggactcgtaa ccatggatca tcatgctcgt catgatatca atgttggcac aacacaggca 33780
cacgtgcata cacttcctca ggattacaag ctcctcccgc gttagaacca tatcccaggg 33840
aacaacccat tcctgaatca gcgtaaatcc cacactgcag ggaagacctc gcacgtaact 33900
cacgttgtgc attgtcaaag tgttacattc gggcagcagc ggatgatcct ccagtatggt 33960
agcgcgggtt tctgtctcaa aaggaggtag acgatcccta ctgtacggag tgcgccgaga 34020
caaccgagat cgtgttggtc gtagtgtcat gccaaatgga acgccggacg tagtcatatt 34080
tcctgaagca aaaccaggtg cgggcgtgac aaacagatct gcgtctccgg tctcgccgct 34140
tagatcgctc tgtgtagtag ttgtagtata tccactctct caaagcatcc aggcgccccc 34200
tggcttcggg ttctatgtaa actccttcat gcgccgctgc cctgataaca tccaccaccg 34260
cagaataagc cacacccagc caacctacac attcgttctg cgagtcacac acgggaggag 34320
cgggaagagc tggaagaacc atgttttttt ttttattcca aaagattatc caaaacctca 34380
aaatgaagat ctattaagtg aacgcgctcc cctccggtgg cgtggtcaaa ctctacagcc 34440
aaagaacaga taatggcatt tgtaagatgt tgcacaatgg cttccaaaag gcaaacggcc 34500
ctcacgtcca agtggacgta aaggctaaac ccttcagggt gaatctcctc tataaacatt 34560
ccagcacctt caaccatgcc caaataattc tcatctcgcc accttctcaa tatatctcta 34620
agcaaatccc gaatattaag tccggccatt gtaaaaatct gctccagagc gccctccacc 34680
ttcagcctca agcagcgaat catgattgca aaaattcagg ttcctcacag acctgtataa 34740
gattcaaaag cggaacatta acaaaaatac cgcgatcccg taggtccctt cgcagggcca 34800

gctgaacata atcgtgcagg tctgcacgga ccagcgcggc cacttccccg ccaggaacct 34860
tgacaaaaga acccacactg attatgacac gcatactcgg agctatgcta accagcgtag 34920
ccccgatgta agctttgttg catgggcggc gatataaaat gcaaggtgct gctcaaaaaa 34980
tcaggcaaag cctcgcgcaa aaaagaaagc acatcgtagt catgctcatg cagataaagg 35040
caggtaagct ccggaaccac cacagaaaaa gacaccattt ttctctcaaa catgtctgcg 35100
ggtttctgca taaacacaaa ataaaataac aaaaaaacat ttaaacatta gaagcctgtc 35160
ttacaacagg aaaaacaacc cttataagca taagacggac tacggccatg ccggcgtgac 35220
cgtaaaaaaa ctggtcaccg tgattaaaaa gcaccaccga cagctcctcg gtcatgtccg 35280
gagtcataat gtaagactcg gtaaacacat caggttgatt catcggtcag tgctaaaaag 35340
cgaccgaaat agcccggggg aatacatacc cgcaggcgta gagacaacat tacagccccc 35400
ataggaggta taacaaaatt aataggagag aaaaacacat aaacacctga aaaaccctcc 35460
tgcctaggca aaatagcacc ctcccgctcc agaacaacat acagcgcttc acagcggcag 35520
cctaacagtc agccttacca gtaaaaaaga aaacctatta aaaaaacacc actcgacacg 35580
gcaccagctc aatcagtcac agtgtaaaaa agggccaagt gcagagcgag tatatatagg 35640
actaaaaaat gacgtaacgg ttaaagtcca caaaaaacac ccagaaaacc gcacgcgaac 35700
ctacgcccag aaacgaaagc caaaaaaccc acaacttcct caaatcgtca cttccgtttt 35760
cccacgttac gtaacttccc atttaagaa aactacaatt cccaacacat acaagttact 35820
ccgccctaaa acctacgtca cccgccccgt tcccacgccc cgcgccacgt cacaaactcc 35880
acccctcat tatcatattg gcttcaatcc aaaataaggt atattattga tgatg 35935

<210> 9
<211> 35935
<212> DNA
<213> Adenovirus serotype 5

<400> 9
catcatcaat aatatacctt attttggatt gaagccaata tgataatgag ggggtggagt 60
ttgtgacgtg gcgcggggcg tgggaacggg gcgggtgacg tagtagtgtg gcggaagtgt 120
gatgttgcaa gtgtggcgga acacatgtaa gcgacggatg tggcaaaagt gacgtttttg 180
gtgtgcgccg gtgtacacag gaagtgacaa ttttcgcgcg gttttaggcg gatgttgtag 240
taaatttggg cgtaaccgag taagatttgg ccattttcgc gggaaaactg aataagagga 300
agtgaaatct gaataatttt gtgttactca tagcgcgtaa tatttgtcta gggccgcggg 360
gactttgacc gtttacgtgg agactcgccc aggtgttttt ctcaggtgtt ttccgcgttc 420
cgggtcaaag ttggcgtttt attattatag tcagctgacg tgtagtgtat ttatacccgg 480
tgagttcctc aagaggccac tcttgagtgc cagcgagtag agttttctcc tccgagccgc 540
tccgacaccg ggactgaaaa tgagacatat tatctgccac ggaggtgtta ttaccgaaga 600
aatggccgcc agtcttttgg accagctgat cgaagaggta ctggctgata atcttccacc 660
tcctagccat tttgaaccac ctacccttca cgaactgtat gatttagacg tgacggcccc 720
cgaagatccc aacgaggagg cggtttcgca gatttttccc gactctgtaa tgttggcggt 780
gcaggaaggg attgacttac tcacttttcc gccggcgccc ggttctccgg agccgcctca 840
cctttcccgg cagcccgagc agccggagca gagagccttg ggtccggttt ctatgccaaa 900
ccttgtaccg gaggtgatcg atcttacctg ccacgaggct ggctttccac ccagtgacga 960
cgaggatgaa gagggtgagg agtttgtgtt agattatgtg gagcaccccg ggcacggttg 1020
caggtcttgt cattatcacc ggaggaatac gggggaccca gatattatgt gttcgctttg 1080
ctatatgagg acctgtggca tgtttgtcta cagtaagtga aaattatggg cagtgggtga 1140
tagagtggtg ggtttggtgt ggtaattttt tttttaattt ttacagtttt gtggtttaaa 1200
gaattttgta ttgtgatttt tttaaaaggt cctgtgtctg aacctgagcc tgagcccgag 1260
ccagaaccgg agcctgcaag acctacccgc cgtcctaaaa tggcgcctgc tatcctgaga 1320
cgcccgacat cacctgtgtc tagagaatgc aatagtagta cggatagctg tgactccggt 1380
ccttctaaca cacctcctga gatacacccg gtggtcccgc tgtgccccat taaaccagtt 1440
gccgtgagag ttggtgggcg tcgccaggct gtggaatgta tcgaggactt gcttaacgag 1500
cctgggcaac ctttggactt gagctgtaaa cgccccaggc cataaggtgt aaacctgtga 1560
ttgcgtgtgt ggttaacgcc tttgtttgct gaatgagttg atgtaagttt aataaagggt 1620
gagataatgt ttaacttgca tggcgtgtta aatggggcgg ggcttaaagg gtatataatg 1680
cgccgtgggc taatcttggt tacatctgac ctcatggagg cttgggagtg tttggaagat 1740

```
ttttctgctg tgcgtaactt gctggaacag agctctaaca gtacctcttg gttttggagg   1800
tttctgtggg gctcatccca ggcaaagtta gtctgcagaa ttaaggagga ttacaagtgg   1860
gaatttgaag agcttttgaa atcctgtggt gagctgtttg attctttgaa tctgggtcac   1920
caggcgcttt tccaagagaa ggtcatcaag actttggatt tttccacacc ggggcgcgct   1980
gcggctgctg ttgctttttt gagttttata aaggataaat ggagcgaaga aacccatctg   2040
agcggggggt acctgctgga ttttctggcc atgcatctgt ggagagcggt tgtgagacac   2100
aagaatcgcc tgctactgtt gtcttccgtc cgcccggcga taataccgac ggaggagcag   2160
cagcagcagc aggaggaagc caggcggcgg cggcaggagc agagcccatg gaacccgaga   2220
gccggcctgg accctcggga atgaatgttg tacaggtggc tgaactgtat ccagaactga   2280
gacgcatttt gacaattaca gaggatgggc aggggctaaa gggggtaaag agggagcggg   2340
gggcttgtga ggctacagag gaggctagga atctagcttt tagcttaatg accagacacc   2400
gtcctgagtg tattactttt caacagatca aggataattg cgctaatgag cttgatctgc   2460
tggcgcagaa gtattccata gagcagctga ccacttactg gctgcagcca ggggatgatt   2520
ttgaggaggc tattagggta tatgcaaagg tggcacttag gccagattgc aagtacaaga   2580
tcagcaaact tgtaaatatc aggaattgtt gctacatttc tgggaacggg gccgaggtgg   2640
agatagatac ggaggatagg gtggccttta gatgtagcat gataaatatg tggccggggg   2700
tgcttggcat ggacggggtg gttattatga atgtaaggtt tactggcccc aattttagcg   2760
gtacggtttt cctggccaat accaacctta tcctacacgg tgtaagcttc tatgggttta   2820
acaatacctg tgtggaagcc tggaccgatg taagggttcg gggctgtgcc ttttactgct   2880
gctggaaggg ggtggtgtgt cgccccaaaa gcagggcttc aattaagaaa tgcctctttg   2940
aaaggtgtac cttgggtatc ctgtctgagg gtaactccag ggtgcgccac aatgtggcct   3000
ccgactgtgg ttgcttcatg ctagtgaaaa gcgtggctgt gattaagcat aacatggtat   3060
gtggcaactg cgaggacagg gcctctcaga tgctgacctg ctcggacggc aactgtcacc   3120
tgctgaagac cattcacgta gccagccact ctcgcaaggc ctggccagtg tttgagcata   3180
acatactgac ccgctgttcc ttgcatttgg gtaacaggag gggggtgttc ctaccttacc   3240
aatgcaattt gagtcacact aagatattgc ttgagcccga gagcatgtcc aaggtgaacc   3300
tgaacggggt gtttgacatg accatgaaga tctggaaggt gctgaggtac gatgagaccc   3360
gcaccaggtg cagaccctgc gagtgtggcg gtaaacatat taggaaccag cctgtgatgc   3420
tggatgtgac cgaggagctg aggcccgatc acttggtgct ggcctgcacc cgcgctgagt   3480
ttggctctag cgatgaagat acagattgag gtactgaaat gtgtgggcgt ggcttaaggg   3540
tgggaaagaa tatataaggt gggggtctta tgtagttttg tatctgtttt gcagcagccg   3600
ccgccgccat gagcaccaac tcgtttgatg gaagcattgt gagctcatat ttgacaacgc   3660
gcatgccccc atgggccggg gtgcgtcaga atgtgatggg ctccagcatt gatggtcgcc   3720
ccgtcctgcc cgcaaactct actaccttga cctacgagac cgtgtctgga acgccgttgg   3780
agactgcagc ctccgccgcc gcttcagccg ctgcagccac cgcccgcggg attgtgactg   3840
actttgcttt cctgagcccg cttgcaagca gtgcagcttc ccgttcatcc gcccgcgatg   3900
acaagttgac ggctcttttg gcacaattgg attctttgac ccgggaactt aatgtcgttt   3960
ctcagcagct gttggatctg cgccagcagg tttctgccct gaaggcttcc tcccctccca   4020
atgcggttta aaacataaat aaaaaaccag actctgtttg gatttggatc aagcaagtgt   4080
cttgctgtct ttatttaggg gttttgcgcg cgcggtaggc ccgggaccag cggtctcggt   4140
cgttgagggt cctgtgtatt ttttccagga cgtggtaaag gtgactctgg atgttcagat   4200
acatgggcat aagcccgtct ctggggtgga ggtagcacca ctgcagagct tcatgctgcg   4260
gggtggtgtt gtagatgatc cagtcgtagc aggagcgctg ggcgtggtgc ctaaaaatgt   4320
ctttcagtag caagctgatt gccaggggca ggcccttggt gtaagtgttt acaaagcggt   4380
taagctggga tgggtgcata cgtggggata tgagatgcat cttggactgt atttttaggt   4440
tggctatgtt cccagccata tccctccggg gattcatgtt gtgcagaacc accagcacag   4500
tgtatccggt gcacttggga aatttgtcat gtagcttaga aggaaatgcg tggaagaact   4560
tggagacgcc cttgtgacct ccaagatttt ccatgcattc gtccataatg atggcaatgg   4620
gcccacgggc ggcggcctgg gcgaagatat ttctgggatc actaacgtca tagttgtgtt   4680
ccaggatgag atcgtcatag gccattttta caaagcgcgg gcggagggtg ccagactgcg   4740
gtataatggt tccatccggc ccaggggcgt agttaccctc acagatttgc atttcccacg   4800
ctttgagttc agatgggggg atcatgtcta cctgcggggc gatgaagaaa acggtttccg   4860
gggtagggga gatcagctgg gaagaaagca ggttcctgag cagctgcgac ttaccgcagc   4920
cggtgggccc gtaaatcaca cctattaccg ggtgcaactg gtagttaaga gagctgcagc   4980
tgccgtcatc cctgagcagg ggggccactt cgttaagcat gtccctgact cgcatgtttt   5040
```

```
ccctgaccaa atccgccaga aggcgctcgc cgcccagcga tagcagttct tgcaaggaag 5100
caaagttttt caacggtttg agaccgtccg ccgtaggcat gcttttgagc gtttgaccaa 5160
gcagttccag gcggtcccac agctcggtca cctgctctac ggcatctcga tccagcatat 5220
ctcctcgttt cgcgggttgg ggcggctttc gctgtacggc agtagtcggt gctcgtccag 5280
acgggccagg gtcatgtctt tccacgggcg cagggtcctc gtcagcgtag tctgggtcac 5340
ggtgaagggg tgcgctccgg gctgcgcgct ggccagggtg cgcttgaggc tggtcctgct 5400
ggtgctgaag cgctgccggt cttcgccctg cgcgtcggcc aggtagcatt tgaccatggt 5460
gtcatagtcc agcccctccg cggcgtggcc cttggcgcgc agcttgccct tggaggaggc 5520
gccgcacgag gggcagtgca gacttttgag ggcgtagagc ttgggcgcga gaaataccga 5580
ttccggggag taggcatccg cgccgcaggc cccgcagacg gtctcgcatt ccacgagcca 5640
ggtgagctct ggccgttcgg ggtcaaaaac caggtttccc ccatgctttt tgatgcgttt 5700
cttacctctg gtttccatga gccggtgtcc acgctcggtg acgaaaaggc tgtccgtgtc 5760
cccgtataca gacttgagag gcctgtcctc gagcggtgtt ccgcggtcct cctcgtatag 5820
aaactcggac cactctgaga caaaggctcg cgtccaggcc agcacgaagg aggctaagtg 5880
ggaggggtag cggtcgttgt ccactagggg gtccactcgc tccagggtgt gaagacacat 5940
gtcgccctct tcggcatcaa ggaaggtgat tggtttgtag gtgtaggcca cgtgaccggg 6000
tgttcctgaa ggggggctat aaaaggggt gggggcgcgt tcgtcctcac tctcttccgc 6060
atcgctgtct gcgagggcca gctgttgggg tgagtactcc ctctgaaaag cgggcatgac 6120
ttctgcgcta agattgtcag tttccaaaaa cgaggaggat ttgatattca cctggcccgc 6180
ggtgatgcct ttgagggtgg ccgcatccat ctggtcagaa aagacaatct ttttgttgtc 6240
aagcttggtg gcaaacgacc cgtagagggc gttggacagc aacttggcga tggagcgcag 6300
ggtttggttt ttgtcgcgat cggcgcgctc cttggccgcg atgtttagct gcacgtattc 6360
gcgcgcaacg caccgccatt cgggaaagac ggtggtgcgc tcgtcgggca ccaggtgcac 6420
gcgccaaccg cggttgtgca gggtgacaag gtcaacgctg gtggctacct ctccgcgtag 6480
gcgctcgttg gtccagcaga ggcggccgcc cttgcgcgag cagaatggcg gtagggggtc 6540
tagctgcgtc tcgtccgggg ggtctgcgtc cacggtaaag accccgggca gcaggcgcgc 6600
gtcgaagtag tctatcttgc atccttgcaa gtctagcgcc tgctgccatg cgcgggcggc 6660
aagcgcgcgc tcgtatgggt tgagtggggg accccatggc atggggtggg tgagcgcgga 6720
ggcgtacatg ccgcaaatgt cgtaaacgta gaggggctct ctgagtattc caagatatgt 6780
agggtagcat cttccaccgc ggatgctggc gcgcacgtaa tcgtatagtt cgtgcgaggg 6840
agcgaggagg tcgggaccga ggttgctacg ggcgggctgc tctgctcgga agactatctg 6900
cctgaagatg gcatgtgagt tggatgatat ggttggacgc tggaagacgt tgaagctggc 6960
gtctgtgaga cctaccgcgt cacgcacgaa ggaggcgtag gagtcgcgca gcttgttgac 7020
cagctcggcg gtgacctgca cgtctagggc gcagtagtcc agggtttcct tgatgatgtc 7080
atacttatcc tgtccctttt ttttccacag ctcgcggttg aggacaaact cttcgcggtc 7140
tttccagtac tcttggatcg gaaacccgtc ggcctccgaa cggtaagagc ctagcatgta 7200
gaactggttg acggcctggt aggcgcagca tccctttct acgggtagcg cgtatgcctg 7260
cgcggccttc cggagcgagg tgtgggtgag cgcaaaggtg tccctgacca tgactttgag 7320
gtactggtat ttgaagtcag tgtcgtcgca tccgccctgc tcccagagca aaaagtccgt 7380
gcgctttttg gaacgcggat ttggcagggc gaaggtgaca tcgttgaaga gtatctttcc 7440
cgcgcgaggc ataaagttgc gtgtgatgcg gaagggtccc ggcacctcgg aacggttgtt 7500
aattacctgg gcggcgagca cgatctcgtc aaagccgttg atgttgtggc ccacaatgta 7560
aagttccaag aagcgcggga tgcccttgat ggaaggcaat tttttaagtt cctcgtaggt 7620
gagctcttca ggggagctga gcccgtgctc tgaaagggcc cagtctgcaa gatgagggtt 7680
ggaagcgacg aatgagctcc acaggtcacg ggccattagc atttgcaggt ggtcgcgaaa 7740
ggtcctaaac tggcgaccta tggccatttt ttctggggtg atgcagtaga aggtaagcgg 7800
gtcttgttcc cagcggtccc atccaaggtt cgcggctagg tctcgcgcgg cagtcactag 7860
aggctcatct ccgccgaact tcatgaccag catgaagggc acgagctgct tcccaaaggc 7920
ccccatccaa gtataggtct ctacatcgta ggtgacaaag agacgctcgg tgcgaggatg 7980
cgagccgatc gggaagaact ggatctcccg ccaccaattg gaggagtggc tattgatgtg 8040
gtgaaagtag aagtccctgc gacgggccga acactcgtgc tggcttttgt aaaaacgtgc 8100
gcagtactgg cagcggtgca cgggctgtac atcctgcacg aggttgacct gacgaccgcg 8160
cacaaggaag cagagtggga atttgagccc ctcgcctggc gggtttggct ggtggtcttc 8220
tacttcggct gcttgtcctt gaccgtctgg ctgctcgagg ggagttacgg tggatcggac 8280
caccacgccg cgcgagccca aagtccagat gtccgcgcgc ggcggtcgga gcttgatgac 8340
```

aacatcgcgc agatgggagc tgtccatggt ctggagctcc cgcggcgtca ggtcaggcgg 8400
gagctcctgc aggtttacct cgcatagacg ggtcagggcg cgggctagat ccaggtgata 8460
cctaatttcc aggggctggt tggtggcggc gtcgatggct tgcaagaggc cgcatccccg 8520
cggcgcgact acggtaccgc gcggcgggcg gtgggccgcg gggtgtcct tggatgatgc 8580
atctaaaagc ggtgacgcgg gcgagccccc ggaggtaggg ggggctccgg acccgccggg 8640
agagggggca ggggcacgtc ggcgccgcgc gcgggcagga gctggtgctg cgcgcgtagg 8700
ttgctggcga acgcgacgac gcggcggttg atctcctgaa tctggcgcct ctgcgtgaag 8760
acgacgggcc cggtgagctt gagcctgaaa gagagttcga cagaatcaat ttcggtgtcg 8820
ttgacggcgg cctggcgcaa aatctcctgc acgtctcctg agttgtcttg ataggcgatc 8880
tcggccatga actgctcgat ctcttcctcc tggagatctc cgcgtccggc tcgctccacg 8940
gtggcggcga ggtcgttgga aatgcgggcc atgagctgcg agaaggcgtt gaggcctccc 9000
tcgttccaga cgcggctgta gaccacgccc ccttcggcat cgcgggcgcg catgaccacc 9060
tgcgcgagat tgagctccac gtgccgggcg aagacggcgt agtttcgcag gcgctgaaag 9120
aggtagttga gggtggtggc ggtgtgttct gccacgaaga agtacataac ccagcgtcgc 9180
aacgtggatt cgttgatatc ccccaaggcc tcaaggcgct ccatggcctc gtagaagtcc 9240
acggcgaagt tgaaaaactg ggagttgcgc gccgacacgg ttaactcctc ctccagaaga 9300
cggatgagct cggcgacagt gtcgcgcacc tcgcgctcaa aggctacagg ggcctcttct 9360
tcttcttcaa tctcctcttc cataagggcc tccccttctt cttcttctgg cggcggtggg 9420
ggaggggga cacggcggcg acgacggcgc accgggaggc ggtcgacaaa gcgctcgatc 9480
atctccccgc ggcgacggcg catggtctcg gtgacggcgc ggccgttctc gcggggggcgc 9540
agttggaaga cgccgcccgt catgtcccgg ttatgggttg gcgggggggct gccatgcggc 9600
agggatacgg cgctaacgat gcatctcaac aattgttgtg taggtactcc gccgccgagg 9660
gacctgagcg agtccgcatc gaccggatcg gaaaacctct cgagaaaggc gtctaaccag 9720
tcacagtcgc aaggtaggct gagcaccgtg gcgggcggca gcgggcggcg gtcggggttg 9780
tttctggcgg aggtgctgct gatgatgtaa ttaaagtagg cggtcttgag acggcggatg 9840
gtcgacagaa gcaccatgtc cttgggtccg gcctgctgaa tgcgcaggcg gtcggccatg 9900
ccccaggctt cgttttgaca tcggcgcagg tctttgtagt agtcttgcat gagcctttct 9960
accggcactt cttcttctcc ttcctcttgt cctgcatctc ttgcatctat cgctgcggcg 10020
gcggcggagt ttggccgtag gtggcgccct cttcctccca tgcgtgtgac cccgaagccc 10080
ctcatcggct gaagcagggc taggtcggcg acaacgcgct cggctaatat ggcctgctgc 10140
acctgcgtga gggtagactg gaagtcatcc atgtccacaa agcggtggta tgcgcccgtg 10200
ttgatggtgt aagtgcagtt ggccataacg gaccagttaa cggtctggtg acccggctgc 10260
gagagctcgg tgtacctgag acgcgagtaa gccctcgagt caaatacgta gtcgttgcaa 10320
gtccgcacca ggtactggta tcccaccaaa aagtgcggcg gcggctggcg gtagaggggc 10380
cagcgtaggg tggccggggc tccgggggcg agatcttcca acataaggcg atgatatccg 10440
tagatgtacc tggacatcca ggtgatgccg gcggcggtgg tggaggcgcg cggaaagtcg 10500
cggacgcggt tccagatgtt gcgcagcggc aaaaagtgct ccatggtcgg gacgctctgg 10560
ccggtcaggc gcgcgcaatc gttgacgctc tagaccgtgc aaaaggagag cctgtaagcg 10620
ggcactcttc cgtggtctgg tggataaatt cgcaagggta tcatggcgga cgaccggggt 10680
tcgagccccg tatccggccg tccgccgtga tccatgcggt taccgcccgc gtgtcgaacc 10740
caggtgtgcg acgtcagaca acgggggagt gctccttttg gcttccttcc aggcgcggcg 10800
gctgctgcgc tagctttttt ggccactggc cgcgcgcagc gtaagcggtt aggctggaaa 10860
gcgaaagcat taagtggctc gctccctgta gccggagggt tattttccaa gggttgagtc 10920
gcgggacccc cggttcgagt ctcggaccgg ccggactgcg gcgaacgggg gtttgcctcc 10980
ccgtcatgca agaccccgct tgcaaattcc tccggaaaca gggacgagcc cctttttttgc 11040
ttttcccaga tgcatccggt gctgcggcag atgcgccccc ctcctcagca gcggcaagag 11100
caagagcagc ggcagacatg cagggcaccc tcccctcctc ctaccgcgtc aggaggggcg 11160
acatccgcgg ttgacgcggc agcagatggt gattacgaac cccgcggcg ccgggcccgg 11220
cactacctgg acttggagga gggcgagggc ctggcgcggc taggagcgcc ctctcctgag 11280
cggtacccaa gggtgcagct gaagcgtgat acgcgtgagg cgtacgtgcc gcggcagaac 11340
ctgtttcgcg accgcgaggg agaggagccc gaggagatgc gggatcgaaa gttccacgca 11400
gggcgcgagc tgcggcatgg cctgaatcgc gagcggttgc tgcgcgagga ggactttgag 11460
cccgacgcgc gaaccgggat tagtcccgcg cgcgcacacg tggcggccgc cgacctggta 11520
accgcatacg agcagacggt gaaccaggag attaactttc aaaaaagctt taacaaccac 11580
gtgcgtacgc ttgtggcgcg cgaggaggtg gctataggac tgatgcatct gtgggacttt 11640

gtaagcgcgc tggagcaaaa cccaaatagc aagccgctca tggcgcagct gttccttata 11700
gtgcagcaca gcagggacaa cgaggcattc agggatgcgc tgctaaacat agtagagccc 11760
gagggccgct ggctgctcga tttgataaac atcctgcaga gcatagtggt gcaggagcgc 11820
agcttgagcc tggctgacaa ggtggccgcc atcaactatt ccatgcttag cctgggcaag 11880
ttttacgccc gcaagatata ccatacccct tacgttccca tagacaagga ggtaaagatc 11940
gaggggttct acatgcgcat ggcgctgaag gtgcttacct tgagcgacga cctgggcgtt 12000
tatcgcaacg agcgcatcca caaggccgtg agcgtgagcc ggcggcgcga gctcagcgac 12060
cgcgagctga tgcacagcct gcaaagggcc ctggctggca cgggcagcgg cgatagagag 12120
gccgagtcct actttgacgc gggcgctgac ctgcgctggg ccccaagccg acgcgccctg 12180
gaggcagctg gggccggacc tgggctggcg gtggcacccg cgcgcgctgg caacgtcggc 12240
ggcgtggagg aatatgacga ggacgatgag tacgagccag aggacggcga gtactaagcg 12300
gtgatgtttc tgatcagatg atgcaagacg caacggaccc ggcggtgcgg gcggcgctgc 12360
agagccagcc gtccggcctt aactccacgg acgactggcg ccaggtcatg gaccgcatca 12420
tgtcgctgac tgcgcgcaat cctgacgcgt tccggcagca gccgcaggcc aaccggctct 12480
ccgcaattct ggaagcggtg gtcccggcgc gcgcaaaccc cacgcacgag aaggtgctgg 12540
cgatcgtaaa cgcgctggcc gaaaacaggg ccatccggcc cgacgaggcc ggcctggtct 12600
acgacgcgct gcttcagcgc gtggctcgtt acaacagcgg caacgtgcag accaacctgg 12660
accggctggt gggggatgtg cgcgaggccg tggcgcagcg tgagcgcgcg cagcagcagg 12720
gcaacctggg ctccatggtt gcactaaacg ccttcctgag tacacagccc gccaacgtgc 12780
cgcggggaca ggaggactac accaactttg tgagcgcact gcggctaatg gtgactgaga 12840
caccgcaaag tgaggtgtac cagtctgggc cagactattt tttccagacc agtagacaag 12900
gcctgcagac cgtaaacctg agccaggctt tcaaaaactt gcaggggctg tggggggtgc 12960
gggctcccac aggcgaccgc gcgaccgtgt ctagcttgct gacgcccaac tcgcgcctgt 13020
tgctgctgct aatagcgccc ttcacggaca gtggcagcgt gtcccgggac acatacctag 13080
gtcacttgct gacactgtac cgcgaggcca taggtcaggc gcatgtggac gagcatactt 13140
tccaggagat tacaagtgtc agccgcgcgc tggggcagga ggacacgggc agcctggagg 13200
caaccctaaa ctacctgctg accaaccggc ggcagaagat cccctcgttg cacagtttaa 13260
acagcgagga ggagcgcatt ttgcgctacg tgcagcagag cgtgagcctt aacctgatgc 13320
gcgacggggt aacgcccagc gtggcgctgg acatgaccgc gcgcaacatg gaaccgggca 13380
tgtatgcctc aaaccggccg tttatcaacc gcctaatgga ctacttgcat cgcgcggccg 13440
ccgtgaaccc cgagtatttc accaatgcca tcttgaaccc gcactggcta ccgccccctg 13500
gtttctacac cgggggattc gaggtgcccg agggtaacga tggattcctc tgggacgaca 13560
tagacgacag cgtgttttcc ccgcaaccgc agaccctgct agagttgcaa cagcgcgagc 13620
aggcagaggc ggcgctgcga aaggaaagct tccgcaggcc aagcagcttg tccgatctag 13680
gcgctgcggc cccgcggtca gatgctagta gcccatttcc aagcttgata gggtctctta 13740
ccagcactcg caccacccgc ccgcgcctgc tgggcgagga ggagtaccta aacaactcgc 13800
tgctgcagcc gcagcgcgaa aaaaacctgc ctccggcatt tcccaacaac gggatagaga 13860
gcctagtgga caagatgagt agatggaaga cgtacgcgca ggagcacagg gacgtgccag 13920
gcccgcgccc gcccacccgt cgtcaaaggc acgaccgtca gcggggtctg gtgtgggagg 13980
acgatgactc ggcagacgac agcagcgtcc tggatttggg agggagtggc aacccgtttg 14040
cgcaccttcg ccccaggctg gggagaatgt tttaaaaaaa aaaaagcatg atgcaaaata 14100
aaaaactcac caaggccatg gcaccgagcg ttggttttct tgtattcccc ttagtatgcg 14160
gcgcgcggcg atgtatgagg aaggtcctcc tccctcctac gagagtgtgg tgagcgcggc 14220
gccagtggcg gcggcgctgg gttctccctt cgatgctccc ctggacccgc cgtttgtgcc 14280
tccgcggtac ctgcggccta ccggggggag aaacagcatc cgttactctg agttggcacc 14340
cctattcgac accacccgtg tgtacctggt ggacaacaag tcaacggatg tggcatccct 14400
gaactaccag aacgaccaca gcaactttct gaccacggtc attcaaaaca atgactacag 14460
cccgggggag gcaagcacac agaccatcaa tcttgacgac cggtcgcact ggggcggcga 14520
cctgaaaacc atcctgcata ccaacatgcc aaatgtgaac gagttcatgt ttaccaataa 14580
gtttaaggcg cgggtgatgg tgtcgcgctt gcctactaag gacaatcagg tggagctgaa 14640
atacgagtgg gtggagttca cgctgcccga gggcaactac tccgagacca tgaccataga 14700
ccttatgaac aacgcgatcg tggagcacta cttgaaagtg ggcagacaga acggggttct 14760
ggaaagcgac atcggggtaa agtttgacac ccgcaacttc agactggggt ttgaccccgt 14820
cactggtctt gtcatgcctg gggtatatac aaacgaagcc ttccatccag acatcatttt 14880
gctgccagga tgcggggtgg acttcaccca cagccgcctg agcaacttgt tgggcatccg 14940

caagcggcaa cccttccagg agggctttag gatcacctac gatgatctgg agggtggtaa 15000
cattcccgca ctgttggatg tggacgccta ccaggcgagc ttgaaagatg acaccgaaca 15060
gggcgggggt ggcgcaggcg gcagcaacag cagtggcagc ggcgcggaag agaactccaa 15120
cgcggcagcc gcggcaatgc agccggtgga ggacatgaac gatcatgcca ttcgcggcga 15180
cacctttgcc acacgggctg aggagaagcg cgctgaggcc gaagcagcgg ccgaagctgc 15240
cgcccccgct gcgcaacccg aggtcgagaa gcctcagaag aaaccggtga tcaaacccct 15300
gacagaggac agcaagaaac gcagttacaa cctaataagc aatgacagca ccttcaccca 15360
gtaccgcagc tggtaccttg catacaacta cggcgaccct cagaccggaa tccgctcatg 15420
gaccctgctt tgcactcctg acgtaacctg cggctcggag caggtctact ggtcgttgcc 15480
agacatgatg caagaccccg tgaccttccg ctccacgcgc cagatcagca actttccggt 15540
ggtgggcgcc gagctgttgc ccgtgcactc caagagcttc tacaacgacc aggccgtcta 15600
ctcccaactc atccgccagt ttacctctct gacccacgtg ttcaatcgct ttcccgagaa 15660
ccagattttg gcgcgcccgc cagcccccac catcaccacc gtcagtgaaa acgttcctgc 15720
tctcacagat cacgggacgc taccgctgcg caacagcatc ggaggagtcc agcgagtgac 15780
cattactgac gccagacgcc gcacctgccc ctacgtttac aaggccctgg gcatagtctc 15840
gccgcgcgtc ctatcgagcc gcactttttg agcaagcatg tccatcctta tatcgcccag 15900
caataacaca ggctggggcc tgcgcttccc aagcaagatg tttggcgggg ccaagaagcg 15960
ctccgaccaa cacccagtgc gcgtgcgcgg gcactaccgc gcgccctggg gcgcgcacaa 16020
acgcggccgc actgggcgca ccaccgtcga tgacgccatc gacgcggtgg tggaggaggc 16080
gcgcaactac acgcccacgc cgccaccagt gtccacagtg gacgcggcca ttcagaccgt 16140
ggtgcgcgga gcccggcgct atgctaaaat gaagagacgg cggaggcgcg tagcacgtcg 16200
ccaccgccgc cgacccggca ctgccgccca acgcgcggcg gcggccctgc ttaaccgcgc 16260
acgtcgcacc ggccgacggg cggccatgcg ggccgctcga aggctggccg cgggtattgt 16320
cactgtgccc cccaggtcca ggcgacgagc ggccgccgca gcagccgcgg ccattagtgc 16380
tatgactcag ggtcgcaggg gcaacgtgta ttgggtgcgc gactcggtta gcggcctgcg 16440
cgtgcccgtg cgcacccgcc ccccgcgcaa ctagattgca agaaaaaact acttagactc 16500
gtactgttgt atgtatccag cggcggcggc gcgcaacgaa gctatgtcca agcgcaaaat 16560
caaagaagag atgctccagg tcatcgcgcc ggagatctat ggccccccga agaaggaaga 16620
gcaggattac aagccccgaa agctaaagcg ggtcaaaaag aaaaagaaag atgatgatga 16680
tgaacttgac gacgaggtgg aactgctgca cgctaccgcg cccaggcgac gggtacagtg 16740
gaaaggtcga cgcgtaaaac gtgttttgcg acccggcacc accgtagtct ttacgcccgg 16800
tgagcgctcc acccgcacct acaagcgcgt gtatgatgag gtgtacggcg acgaggacct 16860
gcttgagcag gccaacgagc gcctcgggga gtttgcctac ggaaagcggc ataaggacat 16920
gctggcgttg ccgctggacg agggcaaccc aacacctagc ctaaagcccg taacactgca 16980
gcaggtgctg cccgcgcttg caccgtccga agaaaagcgc ggcctaaagc gcgagtctgg 17040
tgacttggca cccaccgtgc agctgatggt acccaagcgc cagcgactgg aagatgtctt 17100
ggaaaaaatg accgtggaac ctgggctgga gcccgaggtc cgcgtgcggc caatcaagca 17160
ggtggcgccg ggactgggcg tgcagaccgt ggacgttcag atacccacta ccagtagcac 17220
cagtattgcc accgccacag agggcatgga gacacaaacg tccccggttg cctcagcggt 17280
ggcggatgcc gcggtgcagg cggtcgctgc ggccgcgtcc aagacctcta cggaggtgca 17340
aacggacccg tggatgtttc gcgtttcagc cccccggcgc ccgcgcggtt cgaggaagta 17400
cggcgccgcc agcgcgctac tgcccgaata tgccctacat ccttccattg cgcctacccc 17460
cggctatcgt ggctacacct accgccccag aagacgagca actacccgac gccgaaccac 17520
cactggaacc cgccgccgcc gtcgccgtcg ccagcccgtg ctggccccga tttccgtgcg 17580
cagggtggct cgcgaaggag gcaggaccct ggtgctgcca acagcgcgct accaccccag 17640
catcgtttaa aagccggtct ttgtggttct tgcagatatg gccctcacct gccgcctccg 17700
tttcccggtg ccgggattcc gaggaagaat gcaccgtagg aggggcatgg ccggccacgg 17760
cctgacgggc ggcatgcgtc gtgcgcacca ccggcggcgg cgcgcgtcgc accgtcgcat 17820
gcgcggcggt atcctgcccc tccttattcc actgatcgcc gcggcgattg gcgccgtgcc 17880
cggaattgca tccgtggcct tgcaggcgca gagacactga ttaaaaacaa gttgcatgtg 17940
gaaaaatcaa aataaaaagt ctggactctc acgctcgctt ggtcctgtaa ctattttgta 18000
gaatggaaga catcaacttt gcgtctctgg ccccgcgaca cggctcgcgc ccgttcatgg 18060
gaaactggca agatatcggc accagcaata tgagcggtgg cgccttcagc tggggctcgc 18120
tgtggagcgg cattaaaaat ttcggttcca ccgttaagaa ctatggcagc aaggcctgga 18180
acagcagcac aggccagatg ctgagggata agttgaaaga gcaaaatttc caacaaaagg 18240

tggtagatgg cctggcctct ggcattagcg gggtggtgga cctggccaac caggcagtgc 18300
aaaataagat taacagtaag cttgatcccc gccctcccgt agaggagcct ccaccggccg 18360
tggagacagt gtctccagag gggcgtggcg aaaagcgtcc gcgcccgac agggaagaaa 18420
ctctggtgac gcaaatagac gagcctccct cgtacgagga ggcactaaag caaggcctgc 18480
ccaccacccg tcccatcgcg cccatggcta ccggagtgct gggccagcac acacccgtaa 18540
cgctggacct gcctcccccc gccgacaccc agcagaaacc tgtgctgcca ggcccgaccg 18600
ccgttgttgt aacccgtcct agccgcgcgt ccctgcgccg cgccgccagc ggtccgcgat 18660
cgttgcggcc cgtagccagt ggcaactggc aaagcacact gaacagcatc gtgggtctgg 18720
gggtgcaatc cctgaagcgc cgacgatgct tctgaatagc taacgtgtcg tatgtgtgtc 18780
atgtatgcgt ccatgtcgcc gccagaggag ctgctgagcc gccgcgcgcc cgctttccaa 18840
gatggctacc ccttcgatga tgccgcagtg gtcttacatg cacatctcgg gccaggacgc 18900
ctcggagtac ctgagccccg ggctggtgca gtttgcccgc gccaccgaga cgtacttcag 18960
cctgaataac aagtttagaa accccacggt ggcgcctacg cacgacgtga ccacagaccg 19020
gtcccagcgt ttgacgctgc ggttcatccc tgtggaccgt gaggatactg cgtactcgta 19080
caaggcgcgg ttcaccctag ctgtgggtga taaccgtgtg ctggacatgg cttccacgta 19140
ctttgacatc cgcggcgtgc tggacagggg ccctactttt aagccctact ctggcactgc 19200
ctacaacgcc ctggctccca agggtgcccc aaatccttgc gaatgggatg aagctgctac 19260
tgctcttgaa ataaacctag aagaagagga cgatgacaac gaagacgaag tagacgagca 19320
agctgagcag caaaaaactc acgtatttgg gcaggcgcct tattctggta taaatattac 19380
aaaggagggt attcaaatag gtgtcgaagg tcaaacacct aaatatgccg ataaaacatt 19440
tcaacctgaa cctcaaatag gagaatctca gtggtacgaa actgaaatta atcatgcagc 19500
tgggagagtc cttaaaaaga ctaccccaat gaaaccatgt tacggttcat atgcaaaacc 19560
cacaaatgaa aatggagggc aaggcattct tgtaaagcaa caaaatggaa agctagaaag 19620
tcaagtggaa atgcaatttt tctcaactac tgaggcgacc gcaggcaatg gtgataactt 19680
gactcctaaa gtggtattgt acagtgaaga tgtagatata gaaaccccag acactcatat 19740
ttcttacatg cccactatta aggaaggtaa ctcacgagaa ctaatgggcc aacaatctat 19800
gcccaacagg cctaattaca ttgcttttag ggacaatttt attggtctaa tgtattacaa 19860
cagcacgggt aatatgggtg ttctggcggg ccaagcatcg cagttgaatg ctgttgtaga 19920
tttgcaagac agaaacacag agctttcata ccagcttttg cttgattcca ttggtgatag 19980
aaccaggtac ttttctatgt ggaatcaggc tgttgacagc tatgatccag atgttagaat 20040
tattgaaaat catggaactg aagatgaact tccaaattac tgctttccac tgggaggtgt 20100
gattaataca gagactctta ccaaggtaaa acctaaaaca ggtcaggaaa atggatggga 20160
aaaagatgct acagaatttt cagataaaaa tgaaataaga gttggaaata attttgccat 20220
ggaaatcaat ctaaatgcca acctgtggag aaatttcctg tactccaaca tagcgctgta 20280
tttgcccgac aagctaaagt acagtccttc caacgtaaaa atttctgata acccaaacac 20340
ctacgactac atgaacaagc gagtggtggc tcccgggtta gtggactgct acattaacct 20400
tggagcacgc tggtcccttg actatatgga caacgtcaac ccatttaacc accaccgcaa 20460
tgctggcctg cgctaccgct caatgttgct gggcaatggt cgctatgtgc ccttccacat 20520
ccaggtgcct cagaagttct ttgccattaa aaacctcctt ctcctgccgg gctcatacac 20580
ctacgagtgg aacttcagga aggatgttaa catggttctg cagagctccc taggaaatga 20640
cctaagggtt gacggagcca gcattaagtt tgatagcatt tgcctttacg ccaccttctt 20700
ccccatggcc cacaacaccg cctccacgct tgaggccatg cttagaaacg acaccaacga 20760
ccagtccttt aacgactatc tctccgccgc caacatgctc taccctatac ccgccaacgc 20820
taccaacgtg cccatatcca tcccctcccg caactgggcg gctttccgcg gctgggcctt 20880
cacgcgcctt aagactaagg aaaccccatc actgggctcg ggctacgacc cttattacac 20940
ctactctggc tctataccct acctagatgg aacctttac ctcaaccaca cctttaagaa 21000
ggtggccatt acctttgact cttctgtcag ctggcctggc aatgaccgcc tgcttacccc 21060
caacgagttt gaaattaagc gctcagttga cggggagggt tacaacgttg cccagtgtaa 21120
catgaccaaa gactggttcc tggtacaaat gctagctaac tacaacattg gctaccaggg 21180
cttctatatc ccagagagct acaaggaccg catgtactcc ttctttagaa acttccagcc 21240
catgagccgt caggtggtgg atgatactaa atacaaggac taccaacagg tgggcatcct 21300
acaccaacac aacaactctg gatttgttgg ctaccttgcc cccaccatgc gcgaaggaca 21360
ggcctaccct gctaacttcc cctatccgct tataggcaag accgcagttg acagcattac 21420
ccagaaaaag tttctttgcg atcgcaccct ttggcgcatc ccattctcca gtaactttat 21480
gtccatgggc gcactcacag acctgggcca aaaccttctc tacgccaact ccgcccacgc 21540

gctagacatg acttttgagg tggatcccat ggacgagccc acccttcttt atgttttgtt 21600
tgaagtcttt gacgtggtcc gtgtgcaccg gccgcaccgc ggcgtcatcg aaaccgtgta 21660
cctgcgcacg cccttctcgg ccggcaacgc cacaacataa agaagcaagc aacatcaaca 21720
acagctgccg ccatgggctc cagtgagcag gaactgaaag ccattgtcaa agatcttggt 21780
tgtgggccat atttttgggg cacctatgac aagcgctttc caggctttgt ttctccacac 21840
aagctcgcct gcgccatagt caatacggcc ggtcgcgaga ctgggggcgt acactggatg 21900
gcctttgcct ggaacccgca ctcaaaaaca tgctacctct ttgagccctt tggcttttct 21960
gaccagcgac tcaagcaggt ttaccagttt gagtacgagt cactcctgcg ccgtagcgcc 22020
attgcttctt cccccgaccg ctgtataacg ctggaaaagt ccacccaaag cgtacagggg 22080
cccaactcgg ccgcctgtgg actattctgc tgcatgtttc tccacgcctt tgccaactgg 22140
ccccaaactc ccatggatca caaccccacc atgaacctta ttaccggggt acccaactcc 22200
atgctcaaca gtccccaggt acagcccacc ctgcgtcgca accaggaaca gctctacagc 22260
ttcctggagc gccactcgcc ctacttccgc agccacagtg cgcagattag gagcgccact 22320
tctttttgtc acttgaaaaa catgtaaaaa taatgtacta gagacacttt caataaaggc 22380
aaatgctttt atttgtacac tctcgggtga ttatttaccc ccacccttgc cgtctgcgcc 22440
gtttaaaaat caaaggggtt ctgccgcgca tcgctatgcg ccactggcag ggacacgttg 22500
cgatactggt gtttagtgct ccacttaaac tcaggcacaa ccatccgcgg cagctcggtg 22560
aagttttcac tccacaggct gcgcaccatc accaacgcgt ttagcaggtc gggcgccgat 22620
atcttgaagt cgcagttggg gcctccgccc tgcgcgcgcg agttgcgata cacagggttg 22680
cagcactgga acactatcag cgccgggtgg tgcacgctgg ccagcacgct cttgtcggag 22740
atcagatccg cgtccaggtc ctccgcgttg ctcagggcga acggagtcaa ctttggtagc 22800
tgccttccca aaaagggcgc gtgcccaggc tttgagttgc actcgcaccg tagtggcatc 22860
aaaaggtgac cgtgcccggt ctgggcgtta ggatacagcg cctgcataaa agccttgatc 22920
tgcttaaaag ccacctgagc ctttgcgcct tcagagaaga acatgccgca agacttgccg 22980
gaaaactgat tggccggaca ggccgcgtcg tgcacgcagc accttgcgtc ggtgttggag 23040
atctgcacca catttcggcc ccaccggttc ttcacgatct tggccttgct agactgctcc 23100
ttcagcgcgc gctgcccgtt ttcgctcgtc acatccattt caatcacgtg ctccttattt 23160
atcataatgc ttccgtgtag acacttaagc tcgccttcga tctcagcgca gcggtgcagc 23220
cacaacgcgc agcccgtggg ctcgtgatgc ttgtaggtca cctctgcaaa cgactgcagg 23280
tacgcctgca ggaatcgccc catcatcgtc acaaaggtct tgttgctggt gaaggtcagc 23340
tgcaacccgc ggtgctcctc gttcagccag gtcttgcata cggccgccag agcttccact 23400
tggtcaggca gtagtttgaa gttcgccttt agatcgttat ccacgtggta cttgtccatc 23460
agcgcgcgcg cagcctccat gcccttctcc cacgcagaca cgatcggcac actcagcggg 23520
ttcatcaccg taatttcact ttccgcttcg ctgggctctt cctcttcctc ttgcgtccgc 23580
ataccacgcg ccactgggtc gtcttcattc agccgccgca ctgtgcgctt acctcctttg 23640
ccatgcttga ttagcaccgg tgggttgctg aaacccacca tttgtagcgc cacatcttct 23700
ctttcttcct cgctgtccac gattacctct ggtgatggcg ggcgctcggg cttgggagaa 23760
gggcgcttct ttttcttctt gggcgcaatg gccaaatccg ccgccgaggt cgatggccgc 23820
gggctgggtg tgcgcggcac cagcgcgtct tgtgatgagt cttcctcgtc ctcggactcg 23880
atacgccgcc tcatccgctt ttttgggggc gcccggggag gcggcggcga cggggacggg 23940
gacgacacgt cctccatggt tgggggacgt cgcgccgcac cgcgtccgcg ctcgggggtg 24000
gtttcgcgct gctcctcttc ccgactggcc atttccttct cctataggca gaaaaagatc 24060
atggagtcag tcgagaagaa ggacagccta accgcccccт ctgagttcgc caccaccgcc 24120
tccaccgatg ccgccaacgc gcctaccacc ttccccgtcg aggcaccccc gcttgaggag 24180
gaggaagtga ttatcgagca ggacccaggt tttgtaagcg aagacgacga ggaccgctca 24240
gtaccaacag aggataaaaa gcaagaccag gacaacgcag aggcaaacga ggaacaagtc 24300
gggcgggggg acgaaaggca tggcgactac ctagatgtgg gagacgacgt gctgttgaag 24360
catctgcagc gccagtgcgc cattatctgc gacgcgttgc aagagcgcag cgatgtgccc 24420
ctcgccatag cggatgtcag ccttgcctac gaacgccacc tattctcacc gcgcgtaccc 24480
cccaaacgcc aagaaaacgg cacatgcgag cccaacccgc gcctcaactt ctaccccgta 24540
tttgccgtgc cagaggtgct tgccacctat cacatctttt tccaaaactg caagataccc 24600
ctatcctgcc gtgccaaccg cagccgagcg gacaagcagc tggccttgcg gcagggcgct 24660
gtcatacctg atatcgcctc gctcaacgaa gtgccaaaaa tctttgaggg tcttggacgc 24720
gacgagaagc gcgcggcaaa cgctctgcaa caggaaaaca gcgaaaatga aagtcactct 24780
ggagtgttgg tggaactcga gggtgacaac gcgcgcctag ccgtactaaa acgcagcatc 24840

gaggtcaccc actttgccta cccggcactt aacctacccc ccaaggtcat gagcacagtc 24900
atgagtgagc tgatcgtgcg ccgtgcgcag cccctggaga gggatgcaaa tttgcaagaa 24960
caaacagagg agggcctacc cgcagttggc gacgagcagc tagcgcgctg gcttcaaacg 25020
cgcgagcctg ccgacttgga ggagcgacgc aaactaatga tggccgcagt gctcgttacc 25080
gtggagcttg agtgcatgca gcggttcttt gctgacccgg agatgcagcg caagctagag 25140
gaaacattgc actacacctt tcgacagggc tacgtacgcc aggcctgcaa gatctccaac 25200
gtggagctct gcaacctggt ctcctacctt ggaattttgc acgaaaaccg ccttgggcaa 25260
aacgtgcttc attccacgct caagggcgag gcgcgccgcg actacgtccg cgactgcgtt 25320
tacttatttc tatgctacac ctggcagacg gccatgggcg tttggcagca gtgcttggag 25380
gagtgcaacc tcaaggagct gcagaaactg ctaaagcaaa acttgaagga cctatggacg 25440
gccttcaacg agcgctccgt ggccgcgcac ctggcggaca tcattttccc cgaacgcctg 25500
cttaaaaccc tgcaacaggg tctgccagac ttcaccagtc aaagcatgtt gcagaacttt 25560
aggaacttta tcctagagcg ctcaggaatc ttgcccgcca cctgctgtgc acttcctagc 25620
gactttgtgc ccattaagta ccgcgaatgc cctccgccgc tttggggcca ctgctacctt 25680
ctgcagctag ccaactacct tgcctaccac tctgacataa tggaagacgt gagcggtgac 25740
ggtctactgg agtgtcactg tcgctgcaac ctatgcaccc cgcaccgctc cctggtttgc 25800
aattcgcagc tgcttaacga aagtcaaatt atcggtacct ttgagctgca gggtccctcg 25860
cctgacgaaa agtccgcggc tccggggttg aaactcactc cggggctgtg gacgtcggct 25920
taccttcgca aatttgtacc tgaggactac cacgcccacg agattaggtt ctacgaagac 25980
caatcccgcc cgccaaatgc ggagcttacc gcctgcgtca ttacccaggg ccacattctt 26040
ggccaattgc aagccatcaa caaagcccgc caagagtttc tgctacgaaa gggacggggg 26100
gtttacttgg acccccagtc cggcgaggag ctcaacccaa tcccccgcc gccgcagccc 26160
tatcagcagc agccgcgggc ccttgcttcc caggatggca cccaaaaaga agctgcagct 26220
gccgccgcca cccacggacg aggaggaata ctgggacagt caggcagagg aggttttgga 26280
cgaggaggag gaggacatga tggaagactg ggagagccta gacgaggaag cttccgaggt 26340
cgaagaggtg tcagacgaaa caccgtcacc ctcggtcgca ttcccctcgc cggcgcccca 26400
gaaatcggca accggttcca gcatggctac aacctccgct cctcaggcgc cgccggcact 26460
gcccgttcgc cgacccaacc gtagatggga caccactgga accagggccg gtaagtccaa 26520
gcagccgccg ccgttagccc aagagcaaca acagcgccaa ggctaccgct catggcgcgg 26580
gcacaagaac gccatagttg cttgcttgca agactgtggg ggcaacatct ccttcgcccg 26640
ccgctttctt ctctaccatc acggcgtggc cttcccccgt aacatcctgc attactaccg 26700
tcatctctac agcccatact gcaccggcgg cagcggcagc ggcagcaaca gcagcggcca 26760
cacagaagca aaggcgaccg gatagcaaga ctctgacaaa gcccaagaaa tccacagcgg 26820
cggcagcagc aggaggagga gcgctgcgtc tggcgcccaa cgaacccgta tcgacccgcg 26880
agcttagaaa caggattttt cccactctgt atgctatatt tcaacagagc aggggccaag 26940
aacaagagct gaaaataaaa aacaggtctc tgcgatccct cacccgcagc tgcctgtatc 27000
acaaaagcga agatcagctt cggcgcacgc tggaagacgc ggaggctctc ttcagtaaat 27060
actgcgcgct gactcttaag gactagtttc gcgccctttc tcaaatttaa gcgcgaaaac 27120
tacgtcatct ccagcggcca cacccggcgc cagcacctgt cgtcagcgcc attatgagca 27180
aggaaattcc cacgccctac atgtggagtt accagccaca aatgggactt gcggctggag 27240
ctgcccaaga ctactcaacc cgaataaact acatgagcgc gggaccccac atgatatccc 27300
gggtcaacgg aatccgcgcc caccgaaacc gaattctctt ggaacaggcg gctattacca 27360
ccacacctcg taataacctt aatccccgta gttggcccgc tgccctggtg taccaggaaa 27420
gtcccgctcc caccactgtg gtacttccca gagacgccca ggccgaagtt cagatgacta 27480
actcaggggc gcagcttgcg ggcggctttc gtcacagggt gcggtcgccc gggcagggta 27540
taactcacct gacaatcaga gggcgaggta ttcagctcaa cgacgagtcg gtgagctcct 27600
cgcttggtct ccgtccggac gggacatttc agatcggcgg cgccggccgt ccttcattca 27660
cgcctcgtca ggcaatccta actctgcaga cctcgtcctc tgagccgcgc tctggaggca 27720
ttggaactct gcaatttatt gaggagtttg tgccatcggt ctactttaac cccttctcgg 27780
gacctcccgg ccactatccg gatcaattta ttcctaactt tgacgcggta aaggactcgg 27840
cggacggcta cgactgaatg ttaagtggag aggcagagca actgcgcctg aaacacctgg 27900
tccactgtcg ccgccacaag tgctttgccc gcgactccgg tgagttttgc tactttgaat 27960
tgcccgagga tcatatcgag ggcccggcgc acggcgtccg gcttaccgcc cagggagagc 28020
ttgcccgtag cctgattcgg gagtttaccc agcgccccct gctagttgag cgggacaggg 28080
gaccctgtgt tctcactgtg atttgcaact gtcctaacct tggattacat caagatcttt 28140

gttgccatct ctgtgctgag tataataaat acagaaatta aaatatactg gggctcctat 28200
cgccatcctg taaacgccac cgtcttcacc cgcccaagca aaccaaggcg aaccttacct 28260
ggtactttta acatctctcc ctctgtgatt tacaacagtt tcaacccaga cggagtgagt 28320
ctacgagaga acctctccga gctcagctac tccatcagaa aaaacaccac cctccttacc 28380
tgccgggaac gtacgagtgc gtcaccggcc gctgcaccac acctaccgcc tgaccgtaaa 28440
ccagactttt tccggacaga cctcaataac tctgtttacc agaacaggag gtgagcttag 28500
aaaaccctta gggtattagg ccaaaggcgc agctactgtg gggtttatga acaattcaag 28560
caactctacg ggctattcta attcaggttt ctctagaatc ggggttgggg ttattctctg 28620
tcttgtgatt ctctttattc ttatactaac gcttctctgc ctaaggctcg ccgcctgctg 28680
tgtgcacatt tgcatttatt gtcagctttt taaacgctgg ggtcgccacc caagatgatt 28740
aggtacataa tcctaggttt actcaccctt gcgtcagccc acggtaccac ccaaaaggtg 28800
gattttaagg agccagcctg taatgttaca ttcgcagctg aagctaatga gtgcaccact 28860
cttataaaat gcaccacaga acatgaaaag ctgcttattc gccacaaaaa caaaattggc 28920
aagtatgctg tttatgctat ttggcagcca ggtgacacta cagagtataa tgttacagtt 28980
ttccagggta aaagtcataa aacttttatg tatacttttc cattttatga aatgtgcgac 29040
attaccatgt acatgagcaa acagtataag ttgtggcccc cacaaaattg tgtggaaaac 29100
actggcactt tctgctgcac tgctatgcta attacagtgc tcgctttggt ctgtacccta 29160
ctctatatta aatacaaaag cagacgcagc tttattgagg aaaagaaaat gccttaattt 29220
actaagttac aaagctaatg tcaccactaa ctgctttact cgctgcttgc aaaacaaatt 29280
caaaaagtta gcattataat tagaatagga tttaaacccc ccggtcattt cctgctcaat 29340
accattcccc tgaacaattg actctatgtg ggatatgctc cagcgctaca accttgaagt 29400
caggcttcct ggatgtcagc atctgacttt ggccagcacc tgtcccgcgg atttgttcca 29460
gtccaactac agcgacccac cctaacagag atgaccaaca caaccaacgc ggccgccgct 29520
accggactta catctaccac aaatacaccc caagtttctg cctttgtcaa taactgggat 29580
aacttgggca tgtggtggtt ctccatagcg cttatgtttg tatgccttat tattatgtgg 29640
ctcatctgct gcctaaagcg caaacgcgcc cgaccaccca tctatagtcc catcattgtg 29700
ctacacccaa acaatgatgg aatccataga ttggacggac tgaaacacat gttcttttct 29760
cttacagtat gattaaatga gacatgattc ctcgagtttt tatattactg acccttgttg 29820
cgcttttttg tgcgtgctcc acattggctg cggtttctca catcgaagta gactgcattc 29880
cagccttcac agtctatttg ctttacggat ttgtcaccct cacgctcatc tgcagcctca 29940
tcactgtggt catcgccttt atccagtgca ttgactgggt ctgtgtgcgc tttgcatatc 30000
tcagacacca tccccagtac agggacagga ctatagctga gcttcttaga attctttaat 30060
tatgaaattt actgtgactt ttctgctgat tatttgcacc ctatctgcgt tttgttcccc 30120
gacctccaag cctcaaagac atatatcatg cagattcact cgtatatgga atattccaag 30180
ttgctacaat gaaaaaagcg atctttccga agcctggtta tatgcaatca tctctgttat 30240
ggtgttctgc agtaccatct tagccctagc tatatatccc taccttgaca ttggctggaa 30300
acgaatagat gccatgaacc acccaacttt ccccgcgccc gctatgcttc cactgcaaca 30360
agttgttgcc ggcggctttg tcccagccaa tcagcctcgc cccacttctc ccaccccccac 30420
tgaaatcagc tactttaatc taacaggagg agatgactga caccctagat ctagaaatgg 30480
acggaattat tacagagcag cgcctgctag aaagacgcag ggcagcggcc gagcaacagc 30540
gcatgaatca agagctccaa gacatggtta acttgcacca gtgcaaaagg ggtatctttt 30600
gtctggtaaa gcaggccaaa gtcacctacg acagtaatac caccggacac cgccttagct 30660
acaagttgcc aaccaagcgt cagaaattgg tggtcatggt gggagaaaag cccattacca 30720
taactcagca ctcggtagaa accgaaggct gcattcactc accttgtcaa ggacctgagg 30780
atctctgcac ccttattaag accctgtgcg gtctcaaaga tcttattccc tttaactaat 30840
aaaaaaaaat aataaagcat cacttactta aaatcagtta gcaaatttct gtccagttta 30900
ttcagcagca cctccttgcc ctcctcccag ctctggtatt gcagcttcct cctggctgca 30960
aactttctcc acaatctaaa tggaatgtca gtttcctcct gttcctgtcc atccgcaccc 31020
actatcttca tgttgttgca gatgaagcgc gcaagaccgt ctgaagatac cttcaacccc 31080
gtgtatccat atgacacgga aaccggtcct ccaactgtgc cttttcttac tcctcccttt 31140
gtatccccca atgggtttca agagagtccc cctggggtac tctctttgcg cctatccgaa 31200
cctctagtta cctccaatgg catgcttgcg ctcaaaatgg gcaacggcct ctctctggac 31260
gaggccggca accttacctc ccaaaatgta accactgtga gcccacctct caaaaaaacc 31320
aagtcaaaca taaacctgga aatatctgca cccctcacag ttacctcaga agccctaact 31380
gtggctgccg ccgcacctct aatggtcgcg ggcaacacac tcaccatgca atcacaggcc 31440

ccgctaaccg tgcacgactc caaacttagc attgccaccc aaggacccct cacagtgtca 31500
gaaggaaagc tagccctgca aacatcaggc cccctcacca ccaccgatag cagtaccctt 31560
actatcactg cctcaccccc tctaactact gccactggta gcttgggcat tgacttgaaa 31620
gagcccattt atacacaaaa tggaaaacta ggactaaagt acggggctcc tttgcatgta 31680
acagacgacc taaacacttt gaccgtagca actggtccag gtgtgactat taataatact 31740
tccttgcaaa ctaaagttac tggagccttg ggttttgatt cacaaggcaa tatgcaactt 31800
aatgtagcag gaggactaag gattgattct caaaacagac gccttatact tgatgttagt 31860
tatccgtttg atgctcaaaa ccaactaaat ctaagactag gacagggccc tctttttata 31920
aactcagccc acaacttgga tattaactac aacaaaggcc tttacttgtt tacagcttca 31980
aacaattcca aaaagcttga ggttaaccta agcactgcca aggggttgat gtttgacgct 32040
acagccatag ccattaatgc aggagatggg cttgaatttg gttcacctaa tgcaccaaac 32100
acaaatcccc tcaaaacaaa aattggccat ggcctagaat ttgattcaaa caaggctatg 32160
gttcctaaac taggaactgg ccttagtttt gacagcacag gtgccattac agtaggaaac 32220
aaaaataatg ataagctaac tttgtggacc acaccagctc catctcctaa ctgtagacta 32280
aatgcagaga aagatgctaa actcactttg gtcttaacaa aatgtggcag tcaaatactt 32340
gctacagttt cagttttggc tgttaaaggc agtttggctc caatatctgg aacagttcaa 32400
agtgctcatc ttattataag atttgacgaa aatggagtgc tactaaacaa ttccttcctg 32460
gacccagaat attggaactt tagaaatgga gatcttactg aaggcacagc ctatacaaac 32520
gctgttggat ttatgcctaa cctatcagct tatccaaaat ctcacggtaa aactgccaaa 32580
agtaacattg tcagtcaagt ttacttaaac ggagacaaaa ctaaacctgt aacactaacc 32640
attacactaa acggtacaca ggaaacagga gacacaactc caagtgcata ctctatgtca 32700
ttttcatggg actggtctgg ccacaactac attaatgaaa tatttgccac atcctcttac 32760
actttttcat acattgccca agaataaaga atcgtttgtg ttatgtttca acgtgtttat 32820
ttttcaattg cagaaaattt caagtcattt ttcattcagt agtatagccc caccaccaca 32880
tagcttatac agatcaccgt accttaatca aactcacaga accctagtat tcaacctgcc 32940
acctccctcc caacacacag agtacacagt cctttctccc cggctggcct taaaaagcat 33000
catatcatgg gtaacagaca tattcttagg tgttatattc cacacggttt cctgtcgagc 33060
caaacgctca tcagtgatat taataaactc cccgggcagc tcacttaagt tcatgtcgct 33120
gtccagctgc tgagccacag gctgctgtcc aacttgcggt tgcttaacgg gcggcgaagg 33180
agaagtccac gcctacatgg gggtagagtc ataatcgtgc atcaggatag ggcggtggtg 33240
ctgcagcagc gcgcgaataa actgctgccg ccgccgctcc gtcctgcagg aatacaacat 33300
ggcagtggtc tcctcagcga tgattcgcac cgcccgcagc ataaggcgcc ttgtcctccg 33360
ggcacagcag cgcaccctga tctcacttaa atcagcacag taactgcagc acagcaccac 33420
aatattgttc aaaatcccac agtgcaaggc gctgtatcca aagctcatgg cggggaccac 33480
agaacccacg tggccatcat accacaagcg caggtagatt aagtggcgac ccctcataaa 33540
cacgctggac ataaacatta cctcttttgg catgttgtaa ttcaccacct cccggtacca 33600
tataaacctc tgattaaaca tggcgccatc caccaccatc ctaaaccagc tggccaaaac 33660
ctgcccgccg gctatacact gcagggaacc gggactggaa caatgacagt ggagagccca 33720
ggactcgtaa ccatggatca tcatgctcgt catgatatca atgttggcac aacacaggca 33780
cacgtgcata cacttcctca ggattacaag ctcctcccgc gttagaacca tatcccaggg 33840
aacaacccat tcctgaatca gcgtaaatcc cacactgcag ggaagacctc gcacgtaact 33900
cacgttgtgc attgtcaaag tgttacattc gggcagcagc ggatgatcct ccagtatggt 33960
agcgcgggtt tctgtctcaa aggaggtag acgatcccta ctgtacggag tgcgccgaga 34020
caaccgagat cgtgttggtc gtagtgtcat gccaaatgga acgccggacg tagtcatatt 34080
tcctgaagca aaaccaggtg cgggcgtgac aaacagatct gcgtctccgg tctcgccgct 34140
tagatcgctc tgtgtagtag ttgtagtata tccactctct caaagcatcc aggcgccccc 34200
tggcttcggg ttctatgtaa actccttcat gcgccgctgc cctgataaca tccaccaccg 34260
cagaataagc cacacccagc caacctacac attcgttctg cgagtcacac acgggaggag 34320
cgggaagagc tggaagaacc atgttttttt ttttattcca aaagattatc caaaacctca 34380
aaatgaagat ctattaagtg aacgcgctcc cctccggtgg cgtggtcaaa ctctacagcc 34440
aaagaacaga taatggcatt tgtaagatgt tgcacaatgg cttccaaaag gcaaacggcc 34500
ctcacgtcca agtggacgta aaggctaaac ccttcagggt gaatctcctc tataaacatt 34560
ccagcacctt caaccatgcc caaataattc tcatctcgcc accttctcaa tatatctcta 34620
agcaaatccc gaatattaag tccggccatt gtaaaaatct gctccagagc gccctccacc 34680
ttcagcctca agcagcgaat catgattgca aaaattcagg ttcctcacag acctgtataa 34740

gattcaaaag cggaacatta acaaaaatac cgcgatcccg taggtccctt cgcagggcca 34800
gctgaacata atcgtgcagg tctgcacgga ccagcgcggc cacttccccg ccaggaacct 34860
tgacaaaaga acccacactg attatgacac gcatactcgg agctatgcta accagcgtag 34920
ccccgatgta agctttgttg catgggcggc gatataaaat gcaaggtgct gctcaaaaaa 34980
tcaggcaaag cctcgcgcaa aaaagaaagc acatcgtagt catgctcatg cagataaagg 35040
caggtaagct ccggaaccac cacagaaaaa gacaccattt ttctctcaaa catgtctgcg 35100
ggtttctgca taaacacaaa ataaaataac aaaaaaacat ttaaacatta gaagcctgtc 35160
ttacaacagg aaaaacaacc cttataagca taagacggac tacggccatg ccggcgtgac 35220
cgtaaaaaaa ctggtcaccg tgattaaaaa gcaccaccga cagctcctcg gtcatgtccg 35280
gagtcataat gtaagactcg gtaaacacat caggttgatt catcggtcag tgctaaaaag 35340
cgaccgaaat agcccggggg aatacatacc cgcaggcgta gagacaacat tacagccccc 35400
ataggaggta taacaaaatt aataggagag aaaaacacat aaacacctga aaaaccctcc 35460
tgcctaggca aaatagcacc ctcccgctcc agaacaacat acagcgcttc acagcggcag 35520
cctaacagtc agccttacca gtaaaaaaga aaacctatta aaaaaacacc actcgacacg 35580
gcaccagctc aatcagtcac agtgtaaaaa agggccaagt gcagagcgag tatatatagg 35640
actaaaaaat gacgtaacgg ttaaagtcca caaaaaacac ccagaaaacc gcacgcgaac 35700
ctacgcccag aaacgaaagc caaaaaaccc acaacttcct caaatcgtca cttccgtttt 35760
cccacgttac gtaacttccc attttaagaa aactacaatt cccaacacat acaagttact 35820
ccgccctaaa acctacgtca cccgccccgt tcccacgccc cgcgccacgt cacaaactcc 35880
accccctcat tatcatattg gcttcaatcc aaaataaggt atattattga tgatg 35935

<210> 10
<211> 5965
<212> DNA
<213> Artificial Sequence

<220>
<223> NSsuboptmut

<400> 10
gccaccatgg cccccatcac cgcctacagc cagcagacca ggggcctgct gggctgcatc 60
atcaccagcc tgaccggacg cgacaagaac caggtggagg gagaggtgca ggtggtgagc 120
accgctaccc agagcttcct ggccacctgc gtgaacggcg tgtgctggac cgtgtaccac 180
ggagccggaa gcaagaccct ggccggaccc aagggcccta tcacccagat gtacaccaat 240
gtggatcagg atctggtggg ctggcaggcc cctcccggag ccaggagcct gacaccctgt 300
acctgtggaa gcagcgacct gtacctggtg acacgccacg ccgatgtgat ccccgtgagg 360
cgcaggggcg attctcgcgg aagcctgctg agccctaggc ccgtgagcta cctgaagggc 420
agcagcggag gacccctgct gtgtccttct ggccatgccg tgggcatttt tcgcgctgcc 480
gtgtgtacca ggggcgtggc caaagccgtg gattttgtgc ccgtggaaag catggagacc 540
accatgcgca gccctgtgtt caccgacaac agctctcccc ctgccgtgcc ccaatcattc 600
caggtggctc acctgcacgc ccctaccgga tctggcaaga gcaccaaggt gcccgctgcc 660
tacgccgctc agggctacaa ggtgctggtg ctgaacccca gcgtggccgc taccctgggc 720
ttcggcgctt acatgagcaa ggcccatggc atcgacccca acatccgcac aggcgtgcgc 780
accatcacca ccggagctcc cgtgacctac agcacctacg gcaagttcct ggccgatgga 840
ggctgcagcg gaggagccta cgacatcatc atctgcgacg agtgccacag caccgacagc 900
accaccatcc tgggcattgg caccgtgctg gatcaggccg aaacagctgg agccaggctg 960
gtggtgctgg ccacagctac ccctcctggc agcgtgaccg tgccccatcc caatatcgag 1020
gaggtggccc tgagcaacac aggcgagatc cccttctacg gcaaggccat ccccatcgag 1080
gccatccgcg gaggcaggca cctgatcttc tgccacagca agaagaagtg cgacgagctg 1140
gctgccaagc tgagcggact gggcatcaac gccgtggcct actacagggg cctggacgtg 1200
tcagtgatcc ccaccatcgg cgatgtggtg gtggtggcca ccgacgccct gatgacaggc 1260
tacaccggag acttcgacag cgtgatcgac tgcaacacct gcgtgaccca gaccgtggac 1320
ttcagcctgg accccacctt caccatcgaa accaccaccg tgcctcagga tgctgtgagc 1380
aggagccaga ggcgcggacg caccggaagg ggcaggcgcg gaatttatcg ctttgtgacc 1440
cctggcgaaa ggccctctgg catgttcgac agcagcgtgc tgtgcgagtg ctacgacgct 1500

ggctgcgctt ggtacgagct gacacccgct gaaaccagcg tgcgcctgcg cgcttatctg 1560
aatacccctg gcctgcccgt gtgtcaggac cacctggagt tctgggagag cgtgttcaca 1620
ggactgaccc acatcgacgc ccatttcctg agccagacca agcaggctgg cgacaacttc 1680
ccctatctgg tggcctatca ggccaccgtg tgtgctaggg cccaagctcc acctccttca 1740
tgggaccaga tgtggaagtg cctgatccgc ctgaagccca ccctgcacgg ccctacccct 1800
ctgctgtacc gcctgggagc cgtgcagaac gaggtgaccc tgacccaccc catcaccaag 1860
tacatcatgg cctgcatgag cgctgatctg gaagtggtga ccagcacctg ggtgctggtg 1920
ggaggcgtgc tggccgctct ggctgcctac tgcctgacca ccggaagcgt ggtgatcgtg 1980
ggacgcatca tcctgagcgg aaggcccgct atcgtgcccg atcgcgagtt cctgtaccag 2040
gagttcgacg agatggagga gtgtgccagc cacctgccct acatcgagca gggcatgcag 2100
ctggccgaac agttcaagca gaaggccctg ggcctgctgc agacagccac caaacaggcc 2160
gaagctgccg ctcccgtggt ggaaagcaag tggagggccc tggagacctt ctgggctaag 2220
cacatgtgga acttcatctc tggcatccag tacctggccg gactgagcac cctgcctggc 2280
aaccccgcta tcgccagcct gatggccttc accgctagca tcacctctcc cctgaccacc 2340
cagagcaccc tgctgttcaa cattctgggc ggatgggtgg ccgctcagct ggcccctcct 2400
tcagctgctt ctgcctttgt gggcgctggc attgccggag ccgctgtggg cagcattggc 2460
ctgggcaaag tgctggtgga tattctggct ggctatggcg ctggcgtggc cggagccctg 2520
gtggccttca aggtgatgag cggagagatg cccagcaccg aggacctggt gaacctgctg 2580
cctgccattc tgagccctgg agccctggtg gtgggcgtgg tgtgtgctgc cattctgagg 2640
cgccatgtgg gacccggaga gggcgctgtg cagtggatga accgcctgat cgccttcgcc 2700
tctcgcggaa accacgtgag ccctacccac tacgtgcctg agagcgacgc cgctgccagg 2760
gtgacccaga tcctgagcag cctgaccatc acccagctgc tgaagcgcct gcaccagtgg 2820
atcaacgagg actgcagcac accctgcagc ggaagctggc tgagggacgt gtgggactgg 2880
atctgcaccg tgctgaccga cttcaagacc tggctgcaga gcaagctgct gccccaactg 2940
cctggcgtgc ccttcttctc atgccagcgc ggatacaagg gcgtgtggag gggcgatggc 3000
atcatgcaga ccacctgtcc ctgcggagcc cagatcacag gccacgtgaa gaacggcagc 3060
atgcgcatcg tgggccctaa gacctgcagc aacacctggc acggcacctt ccccatcaac 3120
gcctacacca ccggaccctg cacacccagc cctgctccca actacagcag ggccctgtgg 3180
agggtggctg ccgaggagta cgtggaggtg accagggtgg gagacttcca ctacgtgacc 3240
ggaatgacca ccgacaacgt gaagtgtccc tgtcaggtgc ccgctcccga attttttacc 3300
gaagtggatg gcgtgcgcct gcatcgctat gcccctgcct gtaggcccct gctgcgcgaa 3360
gaagtgacct tccaggtggg cctgaaccag tacctggtgg gcagccagct gccctgcgag 3420
cctgagcccg atgtggccgt gctgaccagc atgctgaccg accccagcca catcacagcc 3480
gaaaccgcta aaggcgcct ggccagggc tctcctccaa gcctggcctc aagcagcgct 3540
agccagctgt ctgctcccag cctgaaggcc acctgcacca cccaccacgt gagccccgac 3600
gccgacctga tcgaggccaa cctgctgtgg cgccaggaga tgggcggcaa catcacccgc 3660
gtggagagcg agaacaaggt ggtggtgctg gacagcttcg acccccctgcg cgccgaggag 3720
gacgagcgcg aggtgagcgt gcccgccgag atcctgcgca agagcaagaa gttccccgct 3780
gccatgccca tctgggctag acctgattac aaccctcccc tgctggagag ctggaaggac 3840
cctgattacg tgcctccagt ggtgcatggc tgtcctctgc ctcccattaa agcccctcct 3900
attccacctc ctaggcgcaa aggaccgtg gtgctgacag aaagcagcgt gagctctgct 3960
ctggccgaac tggccaccaa gacctttggc agcagcgaga gctctgccgt ggacagcgga 4020
acagccaccg ctctgcctga ccaggccagc gacgacggcg ataagggcag cgatgtggag 4080
agctatagca gcatgcctcc cctggaaggc gaacctggcg atcccgatct gagcgatggc 4140
agctggagca ccgtgagcga agaggccagc gaggacgtgg tgtgttgcag catgagctac 4200
acctggacag gcgctctgat cacaccctgc gctgccgagg agagcaagct gcccatcaac 4260
gccctgagca acagcctgct gaggcaccac aacatggtgt acgccaccac cagcaggtct 4320
gccggactga ggcagaagaa ggtgaccttc gaccgcctgc aggtgctgga cgaccactac 4380
cgcgatgtgc tgaaggagat gaaggccaag gccagcaccg tgaaggccaa gctgctgagc 4440
gtggaggagg cctgcaagct gaccccccc cacagcgcca agagcaagtt cggctacggc 4500
gccaaggacg tgcgcaacct gagcagcaag gccgtgaacc acatccacag cgtgtggaag 4560
gacctgctgg aggacaccgt gacccccatc gacaccacca tcatggccaa gaacgaggtg 4620
ttctgcgtgc agcccgagaa gggcggccgc aagcccgctc gcctgatcgt gttccccgat 4680
ctgggcgtgc gcgtgtgcga gaagatggcc ctgtacgacg tggtgagcac cctgcctcag 4740
gtggtgatgg gctcaagcta cggcttccag tacagccctg gccagcgcgt ggagttcctg 4800

gtgaacacct ggaagagcaa gaagaacccc atgggcttca gctacgacac acgctgcttc 4860
gacagcaccg tgaccgagaa cgacatccgc gtggaggaga gcatctacca gtgctgcgac 4920
ctggcccctg aggccaggca ggccatcaag agcctgaccg agcgcctgta catcggaggc 4980
cctctgacca acagcaaggg acagaactgc ggatacaggc gctgtagggc ctctggcgtg 5040
ctgaccacca gctgtggcaa caccctgacc tgctacctga aggccagcgc tgcctgtcgc 5100
gctgccaagc tgcaggactg caccatgctg gtgaacgccg ctggcctggt ggtgatttgt 5160
gaaagcgctg gcacccagga agatgctgcc agcctgcgcg tgttcaccga ggccatgacc 5220
aggtactctg cccctcccgg agaccccct cagcccgaat acgacctgga gctgatcacc 5280
agctgctcaa gcaacgtgag cgtggctcac gacgccagcg gaaagcgcgt gtactacctg 5340
acacgcgatc ccaccacccc tctggctcgc gctgcctggg aaaccgctcg ccatacaccc 5400
gtgaacagct ggctgggcaa catcatcatg tacgccccta ccctgtgggc tcgcatgatc 5460
ctgatgaccc acttcttcag catcctgctg gctcaggagc agctggagaa ggccctggac 5520
tgccagattt acggcgcttg ctacagcatc gagcccctgg acctgcccca aatcatcgag 5580
cgcctgcacg gcctgtctgc cttcagcctg cacagctaca gccctggcga aattaatcgc 5640
gtggccagct gtctgcgcaa actgggcgtg cctcctctgc gcgtgtggag gcatagggct 5700
aggagcgtga gggctaggct gctgagccag ggaggcaggg ccgctacctg tggaaagtac 5760
ctgttcaact gggccgtgaa gaccaagctg aagctgaccc ctatccctgc cgctagccag 5820
ctggacctga gcggatggtt cgtggctggc tacagcggag gcgacatcta ccacagcctg 5880
tctcgcgctc gccctcgctg gttcatgctg tgcctgctgc tgctgagcgt gggcgtgggc 5940
atctacctgc tgcccaaccg ctaaa 5965

<210> 11
<211> 5965
<212> DNA
<213> Artificial Sequence

<220>
<223> Chimeric NSsuboptmut

<400> 11
gccaccatgg cccccatcac cgcctacagc cagcagaccc gcggcctgct gggctgcatc 60
atcaccagcc tgaccggccg cgacaagaac caggtggagg gcgaggtgca ggtggtgagc 120
accgccaccc agagcttcct ggccacctgc gtgaacggcg tgtgctggac cgtgtaccac 180
ggcgccggca gcaagaccct ggccggcccc aagggcccca tcacccagat gtacaccaac 240
gtggaccagg acctggtggg ctggcaggcc ccccccggcg cccgcagcct gacccccctgc 300
acctgcggca gcagcgacct gtacctggtg acccgccacg ccgacgtgat ccccgtgcgc 360
cgccgcggcg acagccgcgg cagcctgctg agcccccgcc ccgtgagcta cctgaagggc 420
agcagcggcg gccccctgct gtgccccagc ggccacgccg tgggcatctt ccgcgccgcc 480
gtgtgcaccc gcggcgtggc caaggccgtg gacttcgtgc ccgtggagag catggagacc 540
accatgcgca gccccgtgtt caccgacaac agcagccccc ccgccgtgcc ccagagcttc 600
caggtggccc acctgcacgc ccccaccggc agcggcaaga gcaccaaggt gcccgccgcc 660
tacgccgccc agggctacaa ggtgctggtg ctgaacccca gcgtggccgc caccctgggc 720
ttcggcgcct acatgagcaa ggcccacggc atcgacccca acatccgcac cggcgtgcgc 780
accatcacca ccggcgcccc cgtgacctac agcacctacg gcaagttcct ggccgacggc 840
ggctgcagcg gcggcgccta cgacatcatc atctgcgacg agtgccacag caccgacagc 900
accaccatcc tgggcatcgg caccgtgctg gaccaggccg agaccgccgg cgcccgcctg 960
gtggtgctgg ccaccgccac ccccccggc agcgtgaccg tgccccaccc caacatcgag 1020
gaggtggccc tgagcaacac cggcgagatc cccttctacg gcaaggccat ccccatcgag 1080
gccatccgcg gcggccgcca cctgatcttc tgccacagca agaagaagtg cgacgagctg 1140
gccgccaagc tgagcggcct gggcatcaac gccgtggcct actaccgcgg cctggacgtg 1200
agcgtgatcc ccaccatcgg cgacgtggtg gtggtggcca ccgacgccct gatgaccggc 1260
tacaccggcg acttcgacag cgtgatcgac tgcaacacct gcgtgaccca gaccgtggac 1320
ttcagcctgg accccacctt caccatcgag accaccaccg tgccccagga cgccgtgagc 1380
cgcagccagc gccgcggccg caccggccgc ggccgccgcg gcatctaccg cttcgtgacc 1440
cccggcgagc gccccagcgg catgttcgac agcagcgtgc tgtgcgagtg ctacgacgcc 1500

ggctgcgcct ggtacgagct gacccccgcc gagaccagcg tgcgcctgcg cgcctacctg 1560
aacacccccg gcctgcccgt gtgccaggac cacctggagt tctgggagag cgtgttcacc 1620
ggcctgaccc acatcgacgc ccacttcctg agccagacca agcaggccgg cgacaacttc 1680
ccctacctgg tggcctacca ggccaccgtg tgcgcccgcg cccaggcccc ccccccagc 1740
tgggaccaga tgtggaagtg cctgatccgc ctgaagccca ccctgcacgg ccccaccccc 1800
ctgctgtacc gcctgggcgc cgtgcagaac gaggtgaccc tgacccaccc catcaccaag 1860
tacatcatgg cctgcatgag cgccgacctg gaggtggtga ccagcacctg ggtgctggtg 1920
ggcggcgtgc tggccgccct ggccgcctac tgcctgacca ccggcagcgt ggtgatcgtg 1980
ggccgcatca tcctgagcgg ccgccccgcc atcgtgcccg accgcgagtt cctgtaccag 2040
gagttcgacg agatggagga gtgcgccagc cacctgccct acatcgagca gggcatgcag 2100
ctggccgagc agttcaagca gaaggccctg ggcctgctgc agaccgccac caagcaggcc 2160
gaggccgccg cccccgtggt ggagagcaag tggcgcgccc tggagacctt ctgggccaag 2220
cacatgtgga acttcatcag cggcatccag tacctggccg gcctgagcac cctgcccggc 2280
aaccccgcca tcgccagcct gatggccttc accgccagca tcaccagccc cctgaccacc 2340
cagagcaccc tgctgttcaa catcctgggc ggctgggtgg ccgcccagct ggcccccccc 2400
agcgccgcca gcgccttcgt gggcgccggc atcgccggcg ccgccgtggg cagcatcggc 2460
ctgggcaagg tgctggtgga catcctggcc ggctacggcg ccggcgtggc cggcgccctg 2520
gtggccttca aggtgatgag cggcgagatg cccagcaccg aggacctggt gaacctgctg 2580
cccgccatcc tgagccccgg cgccctggtg gtgggcgtgg tgtgcgccgc catcctgcgc 2640
cgccacgtgg gccccggcga gggcgccgtg cagtggatga accgcctgat cgccttcgcc 2700
agccgcggca accacgtgag ccccacccac tacgtgcccg agagcgacgc cgccgcccgc 2760
gtgacccaga tcctgagcag cctgaccatc acccagctgc tgaagcgcct gcaccagtgg 2820
atcaacgagg actgcagcac cccctgcagc ggcagctggc tgcgcgacgt gtgggactgg 2880
atctgcaccg tgctgaccga cttcaagacc tggctgcaga gcaagctgct gccccagctg 2940
cccggcgtgc ccttcttcag ctgccagcgc ggctacaagg gcgtgtggcg cggcgacggc 3000
atcatgcaga ccacctgccc ctgcggcgcc cagatcaccg gccacgtgaa gaacggcagc 3060
atgcgcatcg tgggccccaa gacctgcagc aacacctggc acggcacctt ccccatcaac 3120
gcctacacca ccggcccctg cacccccagc cccgccccca actacagccg cgccctgtgg 3180
cgcgtggccg ccgaggagta cgtggaggtg acccgcgtgg gcgacttcca ctacgtgacc 3240
ggcatgacca ccgacaacgt gaagtgcccc tgccaggtgc ccgcccccga gttcttcacc 3300
gaggtggacg gcgtgcgcct gcaccgctac gcccccgcct gccgccccct gctgcgcgag 3360
gaggtgacct tccaggtggg cctgaaccag tacctggtgg gcagccagct gccctgcgag 3420
cccgagcccg acgtggccgt gctgaccagc atgctgaccg accccagcca catcaccgcc 3480
gagaccgcca agcgccgcct ggcccgcggc agccccccca gcctggccag cagcagcgcc 3540
agccagctga gcgcccccag cctgaaggcc acctgcacca cccaccacgt gagccccgac 3600
gccgacctga tcgaggccaa cctgctgtgg cgccaggaga tgggcggcaa catcacccgc 3660
gtggagagcg agaacaaggt ggtggtgctg gacagcttcg accccctgcg cgccgaggag 3720
gacgagcgcg aggtgagcgt gcccgccgag atcctgcgca agagcaagaa gttccccgct 3780
gccatgccca tctgggctag acctgattac aaccctcccc tgctggagag ctggaaggac 3840
cctgattacg tgcctccagt ggtgcatggc tgtcctctgc ctcccattaa agcccctcct 3900
attccacctc ctaggcgcaa aaggaccgtg gtgctgacag aaagcagcgt gagctctgct 3960
ctggccgaac tggccaccaa gacctttggc agcagcgaga gctctgccgt ggacagcgga 4020
acagccaccg ctctgcctga ccaggccagc gacgacggcg ataagggcag cgatgtggag 4080
agctatagca gcatgcctcc cctggaaggc gaacctggcg atcccgatct gagcgatggc 4140
agctggagca ccgtgagcga agaggccagc gaggacgtgg tgtgttgcag catgagctac 4200
acctggacag gcgctctgat cacaccctgc gctgccgagg agagcaagct gcccatcaac 4260
gccctgagca acagcctgct gaggcaccac aacatggtgt acgccaccac cagcaggtct 4320
gccggactga ggcagaagaa ggtgaccttc gaccgcctgc aggtgctgga cgaccactac 4380
cgcgatgtgc tgaaggagat gaaggccaag gccagcaccg tgaaggccaa gctgctgagc 4440
gtggaggagg cctgcaagct gacccccccc cacagcgcca agagcaagtt cggctacggc 4500
gccaaggacg tgcgcaacct gagcagcaag gccgtgaacc acatccacag cgtgtggaag 4560
gacctgctgg aggacaccgt gacccccatc gacaccacca tcatggccaa gaacgaggtg 4620
ttctgcgtgc agcccgagaa gggcggccgc aagcccgccc gcctgatcgt gttccccgac 4680
ctgggcgtgc gcgtgtgcga gaagatggcc ctgtacgacg tggtgagcac cctgccccag 4740
gtggtgatgg gcagcagcta cggcttccag tacagccccg gccagcgcgt ggagttcctg 4800

gtgaacacct ggaagagcaa gaagaacccc atgggcttca gctacgacac ccgctgcttc 4860
gacagcaccg tgaccgagaa cgacatccgc gtggaggaga gcatctacca gtgctgcgac 4920
ctggcccccg aggcccgcca ggccatcaag agcctgaccg agcgcctgta catcggcggc 4980
cccctgacca acagcaaggg ccagaactgc ggctaccgcc gctgccgcgc cagcggcgtg 5040
ctgaccacca gctgcggcaa caccctgacc tgctacctga aggccagcgc cgcctgccgc 5100
gccgccaagc tgcaggactg caccatgctg gtgaacgccg ccggcctggt ggtgatctgc 5160
gagagcgccg gcacccagga ggacgccgcc agcctgcgcg tgttcaccga ggccatgacc 5220
cgctacagcg cccccccCgg cgaccccccc cagcccgagt acgacctgga gctgatcacc 5280
agctgcagca gcaacgtgag cgtggcccac gacgccagcg gcaagcgcgt gtactacctg 5340
acccgcgacc ccaccacccc cctggcccgc gccgcctggg agaccgcccg ccacaccccc 5400
gtgaacagct ggctgggcaa catcatcatg tacgcccccа ccctgtgggc ccgcatgatc 5460
ctgatgaccc acttcttcag catcctgctg gcccaggagc agctggagaa ggccctggac 5520
tgccagatct acggcgcctg ctacagcatc gagcccctgg acctgcccca gatcatcgag 5580
cgcctgcacg gcctgagcgc cttcagcctg cacagctaca gccccggcga gatcaaccgc 5640
gtggccagct gcctgcgcaa gctgggcgtg ccccccctgc gcgtgtggcg ccaccgcgcc 5700
cgcagcgtgc gcgcccgcct gctgagccag ggcggccgcg ccgccacctg cggcaagtac 5760
ctgttcaact gggccgtgaa gaccaagctg aagctgaccc ccatccccgc cgccagccag 5820
ctggacctga gcggctggtt cgtggccggc tacagcggcg gcgacatcta ccacagcctg 5880
agccgcgccc gcccccgctg gttcatgctg tgcctgctgc tgctgagcgt gggcgtgggc 5940
atctacctgc tgcccaaccg ctaaa 5965

<210> 12
<211> 10
<212> RNA
<213> Artificial Sequence

<220>
<223> Ribosome binding site

<400> 12
gccaccaugg 10

<210> 13
<211> 49
<212> RNA
<213> Artificial Sequence

<220>
<223> Synthetic polyadenylation signal

<400> 13
aauaaaagau cuuuauuuuc auuagaucug uguguugguu uuuugugug 49

<210> 14
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Additional nucleotides present in pVIJns-NS

<400> 14
tctagagcgt ttaaaccctt aattaagg 28

<210> 15

<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<223> Additional nucleotides present in pV1Jns-NSOPTmut

<400> 15
tttaaatgtt taaac 15

<210> 16
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer

<400> 16
tcgaatcgat acgcgaacct acgc 24

<210> 17
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer

<400> 17
tcgacgtgtc gacttcgaag cgcacaccaa aaacgtc 37